SEARCH REQUEST FORM

Requestor's Name: [illegible] Serial Number: [illegible]

Date: [illegible] Phone: [illegible] Art Unit: [illegible]

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

1) Please search the standard [illegible] structures. Particular emphasis should be placed on the compounds MORAMPTIDE & MORA[illegible]TIDE (see claims 18 + 19)

2) I am also interested in determining if any peptides have been used in the treatment of viral infections (i.e., [illegible] DNA viruses, retroviruses, etc.), particularly as it applies to HIV-1, HIV-2, or SIV (human and simian immunodeficiency viruses)

Thanks

STAFF USE ONLY

Date completed: ________

Searcher: ________

Terminal time: ________

Elapsed time: ________

CPU time: ________

Total time: ________

Number of Searches: ________

Number of Databases: ________

Search Site

____ STIC

____ CM-1

____ Pre-S

Type of Search

____ N.A. Sequence

____ A.A. Sequence

____ Structure

____ Bibliographic

Vendors

____ IG

____ STN

____ Dialog

____ APS

____ Geninfo

____ SDC

____ DARC/Questel

____ Other

PTO-1590 (9-90)

TI Synthetic peptides, compositions containing them, and their use for diagnosis and vaccination for **AIDS** and ARC.
IN Kennedy, Ronald C.; Dreesman, Gordon R.; Essex, Myron
PA Southwest Foundation for Biomedical Research, USA; Harvard College
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

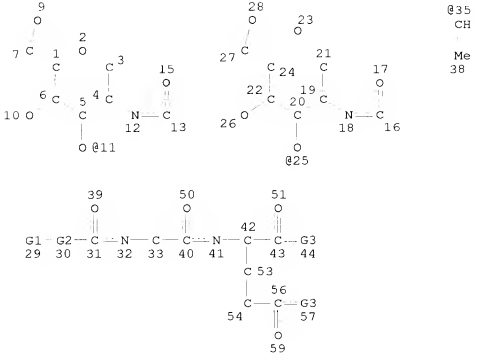
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 8702775	A1	19870507	WO 86-US2234	19861022
W: JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
EP 245362	A1	19871119	EP 86-906660	19861022
EP 245362	B1	19940629		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 63501716	T2	19880714	JP 86-505826	19861022
US 4956273	A	19900911	US 89-331052	19890328
PRAI US 85-790830	19851024			
WO 86-US2234	19861022			
US 88-203609	19880602			

AB Synthetic peptides homologous to the gp 41 and gp 120 subunits of the gp 160 envelope glycoprotein of human T-cell lymphotropic virus type III (HTLV-III) are prepd. for use in detection of antibodies to and vaccination against the viral causative agents of **AIDS** and ARC (**AIDS**-related complex). Hydrophilic regions and regions with .beta.-turns were identified by computer anal. on gp 120, gp 41, and gp 160 as potential immunogenic sites and used as a basis for synthesis of peptides by the Merrifield method. A peptide corresponding to residues 735-752 of gp 120 was conjugated to keyhole limpet hemocyanin for induction of antibody in rabbits. In an assay for diagnosis of **AIDS** by serum antibody detection, an insol. support matrix was coated with a conjugate of this peptide with albumin, incubated with a serum sample, washed, incubated with biotin-labeled goat anti-human Ig followed by an avidin-peroxidase conjugate, H2O2, and a chromogenic substrate.
IT **53678-77-6D**, Muramyl dipeptide, conjugates
74817-61-1D, conjugates
RL: BIOL (Biological study)
(with peptides homologous to **AIDS** virus envelope glycoproteins)

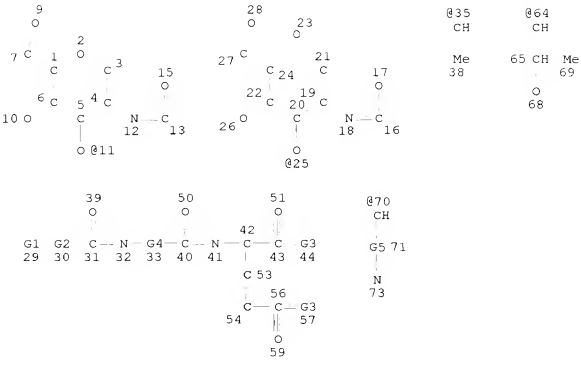
L62 ANSWER 23 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1987:475611 HCAPLUS
DN 107:75611
TI Method and test-kit to detect and/or monitor a pathological condition
IN Spillert, Charles R.; Suval, William A.; Lazaro, Eric J.
PA University of Medicine and Dentistry of New Jersey, USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 8606840	A1	19861120	Wo 86-US1075	19860516
W: AU, BR, DK, JP, NO, US				

```
=> fil reg

FILE 'REGISTRY' ENTERED AT 09:06:53 ON 08 DEC 1998
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 1998 American Chemical Society (ACS)

STRUCTURE FILE UPDATES:   6 DEC  98  HIGHEST RN 215160-44-4
DICTIONARY FILE UPDATES:  7 DEC  98  HIGHEST RN 215160-44-4

TSCA INFORMATION NOW CURRENT THROUGH JUNE 29, 1998

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

=> d stat que l32

L18                 STR
```



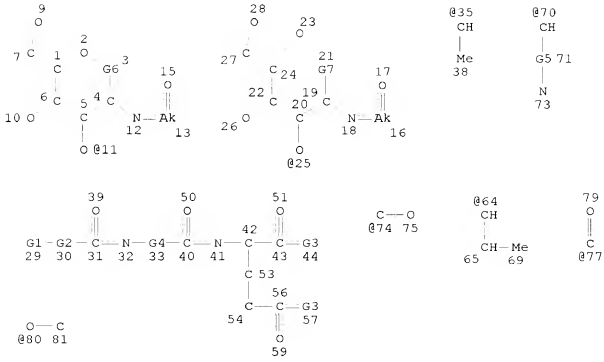

```
VAR G1=11/25
VAR G2=CH2/35
VAR G3=O/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  46

STEREO ATTRIBUTES: NONE
L20             STR
```



VAR G1=11/25
VAR G2=CH2/35
VAR G3=O/N
VAR G4=35/64/70
REP G5=(4-4) CH2
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 53

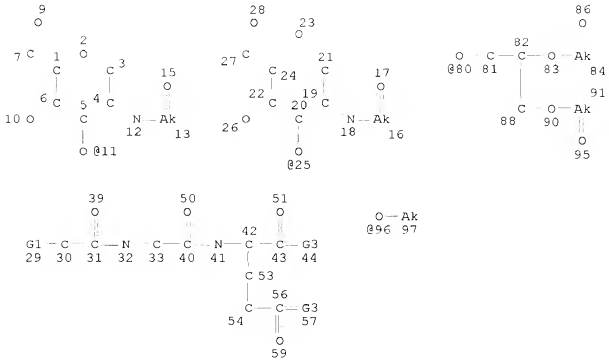
STEREO ATTRIBUTES: NONE
L23 2904 SEA FILE=REGISTRY SSS FUL L18
L24 2373 SEA FILE=REGISTRY SUB=L23 SSS FUL L20
L27 STR



VAR G1=11/25
VAR G2=CH2/35
VAR G3=O/N/80
VAR G4=35/64/70
REP G5=(4-4) CH2
VAR G6=C/74
VAR G7=C/77
NODE ATTRIBUTES:
CONNECT IS M1 RC AT 81
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS E2 C AT 13
ECOUNT IS E2 C AT 16

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 58

STEREO ATTRIBUTES: NONE
L29 130 SEA FILE=REGISTRY SUB=L24 CSS FUL L27
L30 STR



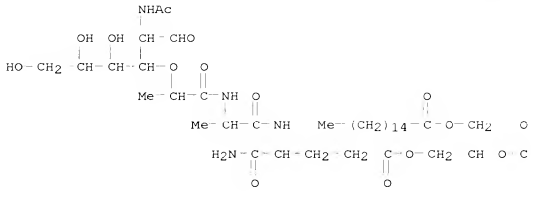
```
VAR G1=11/25
VAR G3=O/N/96/80
NODE ATTRIBUTES:
CONNECT IS M1  RC AT   3
CONNECT IS M1  RC AT  21
CONNECT IS M1  RC AT  30
CONNECT IS M1  RC AT  33
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  56

STEREO ATTRIBUTES: NONE
L32         111 SEA FILE=REGISTRY SUB=L29 CSS FUL L30

100.0% PROCESSED    130 ITERATIONS                          111 ANSWERS
SEARCH TIME: 00.00.01


=> d his 13-14


     (FILE 'HCAPLUS' ENTERED AT 08:20:51 ON 08 DEC 1998)
                E BAHR G/AU
L3           68 S E3-E10
                E VACSYN/PA,CS
L4           18 S E3-E15

=> d his l33-
```

```
     (FILE 'REGISTRY' ENTERED AT 08:23:57 ON 08 DEC 1998)
               SAV L32 PARKIN809C/A

     FILE 'HCAPLUS' ENTERED AT 08:57:12 ON 08 DEC 1998
L33         1350 S L32
L34           37 S L3,L4 AND L33
L35           15 S L33 AND HIV
L36           11 S L33 AND AIDS
L37            4 S L33 AND ACQUIR?(L)IMMUNODEFICIEN?
L38           25 S L33 AND HUMAN(L)IMMUNODEFICIEN?
L39           24 S L38 AND VIRUS?/CW (L) IMMUNODEFICIEN?
L40           24 S L38 AND L39
L41           30 S L35-L40
L42            6 S L34 AND L41

     FILE 'REGISTRY' ENTERED AT 09:01:03 ON 08 DEC 1998
               E MURAMETIDE/CN
L43            1 S E3
               E MURABUTIDE/CN
L44            1 S E3
               E GM-CSF/CN
L45            1 S E3
               E PROTEASE/CN
L46            1 S E3
               E RETROPEP/CN
L47            1 S E4

     FILE 'HCAPLUS' ENTERED AT 09:01:59 ON 08 DEC 1998
L48       105982 S L45 OR L46 OR L47 OR GMCSF OR GM CSF OR COLONY (L) STIM
L49           46 S L48 AND L33
L50            5 S L49 AND L41
L51          128 S L33 AND INTERFERON
L52            7 S L51 AND L41
L53          267 S L33 AND (CYTOKIN? OR LYMPHOKIN?)
L54            6 S L53 AND L41
L55            2 S L33 AND KAPOSI?
L56          119 S L43 OR L44 OR MURAMETIDE OR MURABUTIDE
L57            4 S L56 AND L41
L58           16 S L56 AND L3,L4
L59            3 S L58 AND L41
L60           15 S L42,L50,L52,L54,L55,L57,L59
L61           21 S L41 AND P/DT
L62           23 S L61,L60
               SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 09:06:43 ON 08 DEC 1998
L63           24 S E1-E24

     FILE 'REGISTRY' ENTERED AT 09:06:53 ON 08 DEC 1998

=> d ide can tot l63


L63  ANSWER 1 OF 24  REGISTRY  COPYRIGHT 1998 ACS
RN   127179-83-3  REGISTRY
CN   D-.alpha.-Glutamine, N2-[N-(N-acetylmuramoyl)-L-alanyl]-,
     2,3-bis[(1-oxohexadecyl)oxy]propyl ester, (R)- (9CI)  (CA INDEX
```

= hit cmpds from refs 1-23, see L62

NAME)
DR 159593-41-6, 159652-90-1
MF C54 H98 N4 O15
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

PAGE 1-A



PAGE 1-B

— $(CH_2)_{14}$ — Me

4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 122:23868

REFERENCE 2: 117:118496

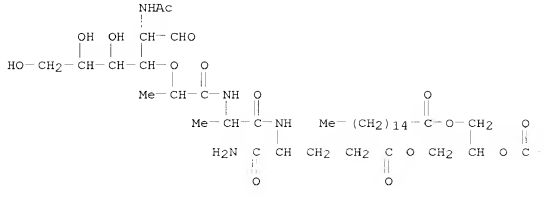
REFERENCE 3: 113:70893

REFERENCE 4: 112:233710

L63 ANSWER 2 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **127088-99-7** REGISTRY
CN D-.alpha.-Glutamine, N2-[N-(N-acetylmuramoyl)-D-alanyl]-, 2,3-bis[(1-oxohexadecyl)oxy]propyl ester, (R)- (9CI) (CA INDEX NAME)
DR 155612-56-9

MF C54 H98 N4 O15
SR CA
LC STN Files: CA, CAPLUS

PAGE 1-A



PAGE 1-B

— $(CH_2)_{14}$ — Me

4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

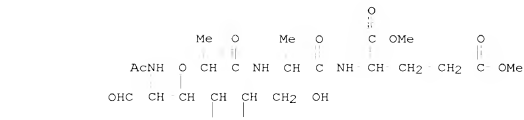
REFERENCE 1: 122:23868

REFERENCE 2: 121:7303

REFERENCE 3: 120:215331

REFERENCE 4: 112:233710

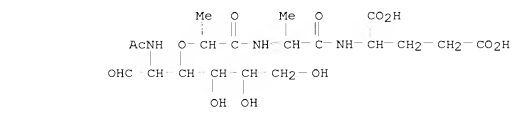
L63 ANSWER 3 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **125637-74-3** REGISTRY
CN D-Glutamic acid, N-[N-(N-acetylisomuramoyl)-L-alanyl]-, dimethyl ester (9CI) (CA INDEX NAME)
MF C21 H35 N3 O12
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 112:112072

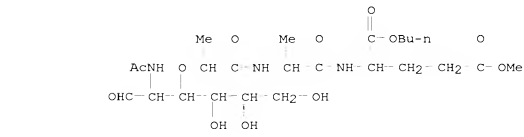
L63 ANSWER 4 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **125637-73-2** REGISTRY
CN D-Glutamic acid, N-[N-(N-acetylisomuramoyl)-L-alanyl]- (9CI) (CA INDEX NAME)
MF C19 H31 N3 O12
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 112:112072

L63 ANSWER 5 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **92512-64-6** REGISTRY
CN D-Glutamic acid, N-[N-(N-acetylmuramoyl)-L-alanyl]-, 1-butyl 5-methyl ester (9CI) (CA INDEX NAME)
DR 110659-06-8
MF C24 H41 N3 O12
LC STN Files: CA, CAPLUS, TOXLIT



5 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:276025

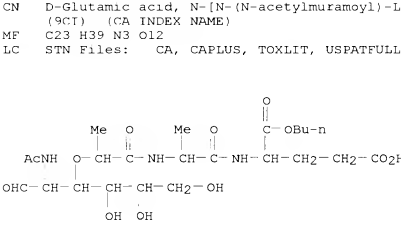
REFERENCE 2: 107:173781

REFERENCE 3: 103:189386

REFERENCE 4: 102:22672

REFERENCE 5: 101:163360

L63 ANSWER 6 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **90159-44-7** REGISTRY
CN D-Glutamic acid, N-[N-(N-acetylmuramoyl)-L-alanyl]-, 1-butyl ester (9CT) (CA INDEX NAME)
MF C23 H39 N3 O12
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



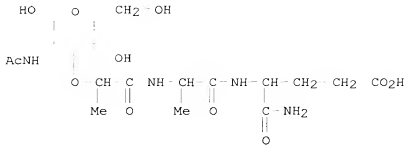
3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:276025

REFERENCE 2: 113:38702

REFERENCE 3: 100:210439

L63 ANSWER 7 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **87420-93-7** REGISTRY
CN D-.alpha.-Glutamine, N2-[N-(N-acetyl-.alpha.-manno-muramoyl)-L-alanyl]- (9CI) (CA INDEX NAME)
MF C19 H32 N4 O11
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 112:112072

REFERENCE 2: 99:158826

L63 ANSWER 8 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **83869-56-1** REGISTRY
CN Colony-stimulating factor 2 (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Colony-stimulating factor II
CN CSF 2
CN GM-CSF
CN Granulocyte-macrophage colony-simulating factor
CN Granulocyte-macrophage colony-stimulating activity
CN Granulocyte-macrophage colony-stimulating factor
CN Granulocyte-macrophage-inducing factor
CN Granulocyte-monocyte colony-stimulating factor
CN Macrophage-granulocyte CSF
CN Macrophage-granulocyte-colony-stimulating factor
MF Unspecified
CI PMS, MAN
PCT Manual registration
LC STN Files: ADISINSIGHT, AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAPLUS, CEN, CHEMCATS, CBNB, CIN, CSCHEM, DRUGPAT, DRUGUPDATES, IPA, MEDLINE, MRCK*, PHAR, PROMT, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
5826 REFERENCES IN FILE CA (1967 TO DATE)
108 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5839 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:321207

REFERENCE 2: 129:321206

REFERENCE 3: 129:314993

REFERENCE 4: 129:314967

REFERENCE 5: 129:314910

REFERENCE 6: 129:314832

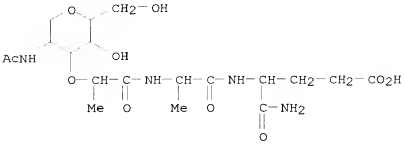
REFERENCE 7: 129:314814

REFERENCE 8: 129:314793

REFERENCE 9: 129:314792

REFERENCE 10: 129:314779

L63 ANSWER 9 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **81638-45-1** REGISTRY
CN D-.alpha.-Glutamine, N2-[N-(N-acetyl-1-deoxymuramoyl)-L-alanyl]- (9CI) (CA INDEX NAME)
DR 84993-83-9
MF C19 H32 N4 O10
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

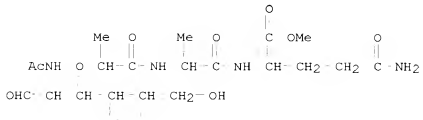
REFERENCE 1: 112:112074

REFERENCE 2: 105:170442

REFERENCE 3: 98:126598

REFERENCE 4: 96:200171

L63 ANSWER 10 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **79787-27-2** REGISTRY
CN D-Glutamine, N2-[N-(N-acetylmuramoyl)-L-alanyl]-, methyl ester (9CI) (CA INDEX NAME)
DR 87349-46-0
MF C20 H34 N4 O11
LC STN Files: CA, CANCERLIT, CAPLUS, EMBASE, MEDLINE, TOXLINE, TOXLIT, USPATFULL



6 REFERENCES IN FILE CA (1967 TO DATE)
6 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 126:1184

REFERENCE 2: 108:187197

REFERENCE 3: 101:183905

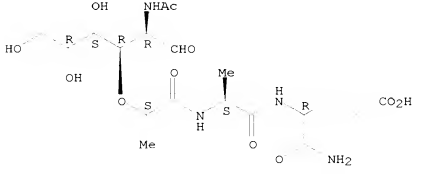
REFERENCE 4: 100:114574

REFERENCE 5: 99:156529

REFERENCE 6: 96:471

L63 ANSWER 11 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **76498-00-5** REGISTRY
CN D-.alpha.-Glutamine, N2-[N-(N-acetyl-D-galacto-isomuramoyl)-L-alanyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H32 N4 O11
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

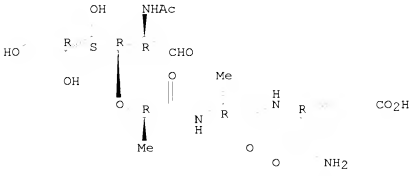
REFERENCE 1: 112:112072

REFERENCE 2: 95:25635

L63 ANSWER 12 OF 24 REGISTRY COPYRIGHT 1998 ACS

RN **76497-96-6** REGISTRY
CN D-.alpha.-Glutamine, N2-[N-(N-acetyl-D-galacto-muramoyl)-D-alanyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H32 N4 O11
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.



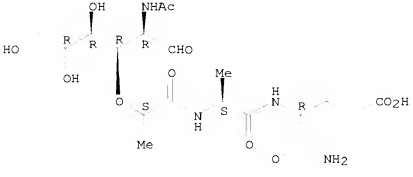
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 112:112072

REFERENCE 2: 95:25635

L63 ANSWER 13 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **76465-71-9** REGISTRY
CN D-.alpha.-Glutamine, N2-[N-(N-acetylisomuramoyl)-L-alanyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H32 N4 O11
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.



4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 122:161318

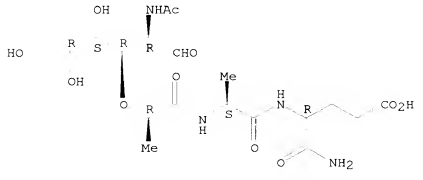
REFERENCE 2: 112:112072

REFERENCE 3: 95:25635

REFERENCE 4: 94:66050

L63 ANSWER 14 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **75283-24-8** REGISTRY
CN D-.alpha.-Glutamine, N2-[N-(N-acetyl-D-galacto-muramoyl)-L-alanyl]-
(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H32 N4 O11
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.



9 REFERENCES IN FILE CA (1967 TO DATE)
9 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 112:112072

REFERENCE 2: 107:190333

REFERENCE 3: 100:66286

REFERENCE 4: 98:126607

REFERENCE 5: 97:174449

REFERENCE 6: 96:33017

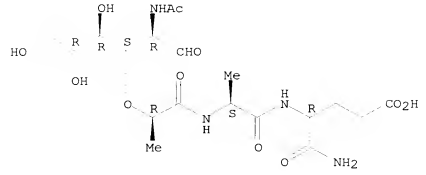
REFERENCE 7: 96:7051

REFERENCE 8: 95:25635

REFERENCE 9: 93:184104

L63 ANSWER 15 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **75283-22-6** REGISTRY
CN D-.alpha.-Glutamine, N2-[N-(N-acetyl-D-allo-muramoyl)-L-alanyl]-
(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H32 N4 O11
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.



12 REFERENCES IN FILE CA (1967 TO DATE)
12 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 112:112072

REFERENCE 2: 107:190333

REFERENCE 3: 105:40958

REFERENCE 4: 103:158639

REFERENCE 5: 100:66286

REFERENCE 6: 98:126607

REFERENCE 7: 97:174449

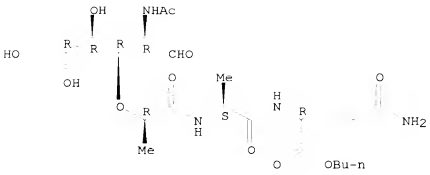
REFERENCE 8: 96:33017

REFERENCE 9: 96:7051

REFERENCE 10: 95:25635

L63 ANSWER 16 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **74817-61-1** REGISTRY
CN D-Glutamine, N-(N-acetylmuramoyl)-L-alanyl-, butyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN D-Glutamine, N2-[N-(N-acetylmuramoyl)-L-alanyl]-, butyl ester
OTHER NAMES:
CN Murabutide
FS STEREOSEARCH
DR 83504-22-7, 87370-60-3
MF C23 H40 N4 O11
LC STN Files: ADISINSIGHT, ANABSTR, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAPLUS, CASREACT, DDFU, DRUGPAT, DRUGU, EMBASE, MEDLINE, PHAR, PROMT, TOXLINE, TOXLIT, USAN, USPATFULL
Other Sources: WHO

Absolute stereochemistry.



96 REFERENCES IN FILE CA (1967 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
96 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:226238

REFERENCE 2: 128:30028

REFERENCE 3: 128:10060

REFERENCE 4: 125:265378

REFERENCE 5: 125:123683

REFERENCE 6: 125:76342

REFERENCE 7: 125:55903

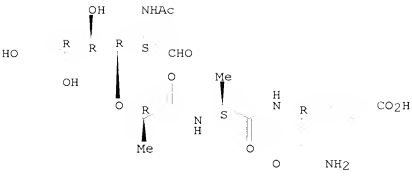
REFERENCE 8: 125:26240

REFERENCE 9: 124:340332

REFERENCE 10: 124:317852

L63 ANSWER 17 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **69351-74-2** REGISTRY
CN D-.alpha.-Glutamine, N2-[N-(N-acetyl-D-manno-muramoyl)-L-alanyl]-
(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H32 N4 O11
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.



6 REFERENCES IN FILE CA (1967 TO DATE)
6 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 112:112072

REFERENCE 2: 97:174449

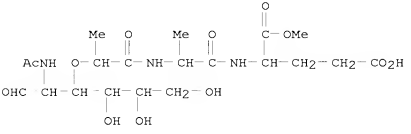
REFERENCE 3: 96:33017

REFERENCE 4: 96:7051

REFERENCE 5: 95:25635

REFERENCE 6: 90:132579

L63 ANSWER 18 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **63555-62-4** REGISTRY
CN D-Glutamic acid, N-[N-(N-acetylmuramoyl)-L-alanyl]-, 1-methyl ester (9CI) (CA INDEX NAME)
MF C20 H33 N3 O12
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



11 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
11 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:276025

REFERENCE 2: 108:137895

REFERENCE 3: 101:50651

REFERENCE 4: 100:210439

REFERENCE 5: 100:114574

REFERENCE 6: 93:43645

REFERENCE 7: 92:215749

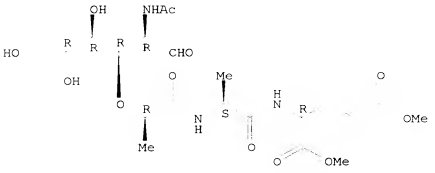
REFERENCE 8: 89:127602

REFERENCE 9: 89:110389

REFERENCE 10: 88:87474

L63 ANSWER 19 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **60355-79-5** REGISTRY
CN D-Glutamic acid, N-[N-(N-acetylmuramoyl)-L-alanyl]-, dimethyl ester (9CI) (CA INDEX NAME)
OTHER NAMES:
CN N-Acetylmuramyl-L-alanyl-D-glutamic acid dimethyl ester
FS STEREOSEARCH
DR 66048-76-8
MF C21 H35 N3 O12
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.



18 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
18 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:55903

REFERENCE 2: 123:276025

REFERENCE 3: 122:23868

REFERENCE 4: 108:137895

REFERENCE 5: 104:161623

REFERENCE 6: 100:114574

REFERENCE 7: 96:471

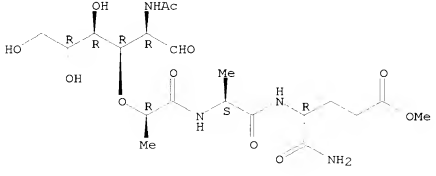
REFERENCE 8: 95:204406

REFERENCE 9: 93:43645

REFERENCE 10: 90:136105

L63 ANSWER 20 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **60355-78-4** REGISTRY
CN D-.alpha.-Glutamine, N-(N-acetylmuramoyl)-L-alanyl-, methyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN D-.alpha.-Glutamine, N2-[N-(N-acetylmuramoyl)-L-alanyl]-, methyl ester
OTHER NAMES:
CN Murametide
CN N-Acetylmuramyl-L-alanyl-D-isoglutamine methyl ester
FS STEREOSEARCH
DR 66009-33-4
MF C20 H34 N4 O11
LC STN Files: BIOSIS, CA, CAPLUS, DDFU, DRUGU, TOXLIT, USPATFULL

Absolute stereochemistry.



35 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
35 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:123683

REFERENCE 2: 125:55903

REFERENCE 3: 125:26240

REFERENCE 4: 124:340332

REFERENCE 5: 124:286389

REFERENCE 6: 123:276025

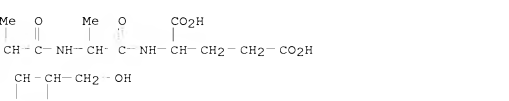
REFERENCE 7: 123:275426

REFERENCE 8: 123:513

REFERENCE 9: 122:312605

REFERENCE 10: 122:48787

L63 ANSWER 21 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **59366-95-9** REGISTRY
CN D-Glutamic acid, N-[N-(N-acetylmuramoyl)-L-alanyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN N-Acetylmuramyl-L-alanyl-D-glutamic acid
DR 66036-56-4
MF C19 H31 N3 O12
LC STN Files: CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXLIT, USPATFULL



44 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
44 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 124:143034

REFERENCE 2: 123:276025

REFERENCE 3: 116:81895

REFERENCE 4: 113:38702

REFERENCE 5: 109:104367

REFERENCE 6: 108:137895

REFERENCE 7: 107:89474

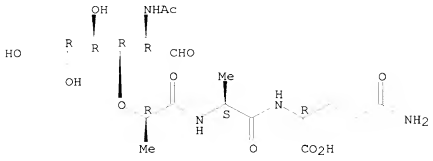
REFERENCE 8: 106:113448

REFERENCE 9: 106:3569

REFERENCE 10: 104:47679

L63 ANSWER 22 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **59309-66-9** REGISTRY
CN D-Glutamine, N-(N-acetylmuramoyl)-L-alanyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN D-Glutamine, N2-[N-(N-acetylmuramoyl)-L-alanyl]-
OTHER NAMES:
CN DV 7401
CN N-Acetylmuramyl-L-alanyl-D-glutamine
FS STEREOSEARCH
MF C19 H32 N4 O11
CI COM
LC STN Files: CA, CAPLUS, CHEMCATS, TOXLIT, USPATFULL

Absolute stereochemistry.



31 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
31 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 126:224271

REFERENCE 2: 124:143034

REFERENCE 3: 120:226704

REFERENCE 4: 116:81895

REFERENCE 5: 113:38702

REFERENCE 6: 109:104367

REFERENCE 7: 108:187197

REFERENCE 8: 108:137895

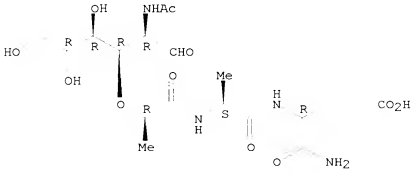
REFERENCE 9: 107:89474

REFERENCE 10: 106:113448

L63 ANSWER 23 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **53678-77-6** REGISTRY
CN D-.alpha.-Glutamine, N-(N-acetylmuramoyl)-L-alanyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN D-.alpha.-Glutamine, N2-[N-(N-acetylmuramoyl)-L-alanyl]-
OTHER NAMES:
CN Acetylmuramyl-L-alanyl-D-isoglutamine
CN MDP
CN Muramyl dipeptide
CN N-(Acetylmuramoyl)alanyl-D-isoglutamine
CN N-(Acetylmuramyl)-L-alanyl-D-isoglutamine
CN N-Acetylmuramyl dipeptide
FS STEREOSEARCH
DR 56769-34-7, 66900-75-2, 66547-81-7, 67461-04-5, 68931-97-5, 74072-38-1, 75720-23-9, 87349-54-0
MF C19 H32 N4 O11
CI COM
LC STN Files: AGRICOLA, AIDSLINE, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU,

DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*,
MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PROMT, RTECS*, TOXLINE,
TOXLIT, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



1194 REFERENCES IN FILE CA (1967 TO DATE)
295 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1196 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:290431

REFERENCE 2: 129:258969

REFERENCE 3: 129:245466

REFERENCE 4: 129:239903

REFERENCE 5: 129:235685

REFERENCE 6: 129:229679

REFERENCE 7: 129:221081

REFERENCE 8: 129:180079

REFERENCE 9: 129:166193

REFERENCE 10: 129:149242

L63 ANSWER 24 OF 24 REGISTRY COPYRIGHT 1998 ACS
RN **9001-92-7** REGISTRY
CN Proteinase (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Actinase
CN Aquatinase E
CN Arginine esterase
CN AS 10
CN Azocaseinase
CN BAPAase

CN Casein endopeptidase
CN Caseinase
CN DA 10
CN DA 10 (enzyme)
CN Endopeptidase
CN Endopeptidase O
CN Endoprotease
CN Endoproteinase
CN Enzylase K 40
CN Enzylon SAL
CN Enzylon SAL 300
CN Enzymes, proteolytic
CN Esteroproteinase
CN Fibrinase
CN GPR protease
CN Growth-related proteinase
CN Isofloridoside phosphate synthase-activating proteinase
CN Leukase
CN Milk-clotting acid proteinase
CN Newlase A
CN Pathogenesis-related proteinase P 69
CN Prolase
CN Protease
CN Protease P3
CN Protease YP-SS
CN Protein p20 proteinase
CN Protein-cleaving enzymes
CN Proteolytic enzyme
CN Proteopol FP-t
CN Samprose F
CN Tamase
CN Thermoase PS
CN ZY 88
DR 9001-93-8, 9012-23-1, 9040-76-0, 125498-72-8, 125752-86-5, 123779-18-0, 124041-97-0, 120038-39-3, 120038-40-6, 105913-13-1, 118901-82-9, 144906-30-9, 143404-30-2, 143404-41-5, 116267-38-0, 117278-03-2, 117698-27-8, 118390-80-0
MF Unspecified
CI COM, MAN
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CBNB, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PLASPEC*, PROMT, RTECS*, TOXLINE, TOXLIT, TULSA, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
25882 REFERENCES IN FILE CA (1967 TO DATE)
301 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
25905 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:321213

REFERENCE 2: 129:321174

REFERENCE 3: 129:317991

REFERENCE 4: 129:317981

REFERENCE 5: 129:316287

REFERENCE 6: 129:316217

REFERENCE 7: 129:315584

REFERENCE 8: 129:315368

REFERENCE 9: 129:315330

REFERENCE 10: 129:315288

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 09:07:57 ON 08 DEC 1998
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1967 - 8 Dec 1998 VOL 129 ISS 24
FILE LAST UPDATED: 8 Dec 1998 (981208/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> d bib abs hitrn tot l62

L62 ANSWER 1 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1998:527193 HCAPLUS
DN 129:166193
TI Therapeutic treatment and prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix
IN Setterstrom, Jean A.; Van Hamont, John E.; Reid, Robert H.; Jacob, Elliot; Jeyanthi, Ramasubbu; Boedeker, Edgar C.; McQueen, Charles E.; Tice, Thomas R.; Roberts, F. Donald; Friden, Phil
PA United States Dept. of the Army, USA; Van Hamont, John E.; et al.
SO PCT Int. Appl., 363 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9832427	A1	19980730	WO 98-US1556	19980127

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,

DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9863175 A1 19980818 AU 98-63175 19980127
PRAI US 97-789734 19970127
WO 98-US1556 19980127

AB Novel burst-free, sustained release biocompatible and biodegradable microcapsules are disclosed which can be programmed to release their active core for variable durations ranging from 1-100 days in an aq. physiol. environment. The microcapsules are comprised of a core of polypeptide or other biol. active agent encapsulated in a matrix of poly(lactide/glycolide) copolymer, which may contain a pharmaceutically acceptable adjuvant, as a blend of upcapped free carboxyl end group and end-capped forms ranging in ratios from 100/0 to 1/99.

IT **53678-77-6D**, Muramyl dipeptide, derivs.
RL: BPR (Biological process); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

L62 ANSWER 2 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1998:239318 HCAPLUS
DN 128:293978
TI Compositions and methods for treating viral infections
IN Gelder, Frank B.
PA Probe International, USA
SO PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9815658	A1	19980416	WO 97-US18257	19971010

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9748131 A1 19980505 AU 97-48131 19971010
PRAI US 96-28194 19961010
WO 97-US18257 19971010

AB Methods and compns. for treatment, diagnosis, and prevention of a virus comprise administering to a patient antibodies which react with regions of viral proteins and result in neutralization of infectivity and inactivation of functionally essential events in the life cycle of the virus. The antibodies recognize viral epitopes which fail to elicit an immune response in man when encountered

through infection or naturally through the environment. The viral epitope mimics epitope region of **HIV**-1 envelope gp120 external glycoprotein, envelope gp41 transmembrane glycoprotein, reverse transcriptase, **protease** p10 or gag precursor. In a preferred embodiment, the invention provides compns. and methods useful in the treatment and diagnosis of **human immunodeficiency** virus (**HIV**) infections.

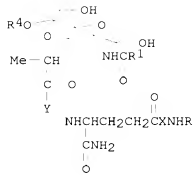
IT **53678-77-6**, Muramyl dipeptide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibodies recognizing **HIV** glycoprotein epitopes or analogs that do not elicit immune response are prepd. for preventing or treating or diagnosing viral or **HIV** infections)

IT **9001-92-7, Protease**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p10; antibodies recognizing **HIV** glycoprotein epitopes or analogs that do not elicit immune response are prepd. for preventing or treating or diagnosing viral or **HIV** infections)

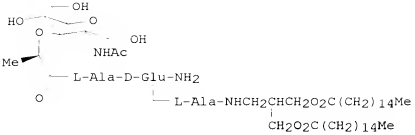
L62 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1997:757027 HCAPLUS
DN 128:13443
TI Preparation of lipophilic muramylpeptide derivatives for treatment of retroviral infection and induction of chemokines
IN Vosika, Gerald J.; Fast, David
PA Endorex Corporation, USA
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9743308	A1	19971120	WO 97-US8146	19970509
	W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9730066	A1	19971205	AU 97-30066	19970509
PRAI	US 96-17248		19960510		
	WO 97-US8146		19970509		

OS MARPAT 128:13443
GI



I



II

AB The invention is directed to methods of inducing the release of at least one chemokine by administering an effective amt. of a muramyl dipeptide compd. (MDP compd.) I [R = CH(O2CR2)O2CR3, CH2CH(O2CR2)CH2O2CR3, CH(CO2R5)(CH2)nNHCOR6, R7; R1 = C1-9 alkyl; R2, R3, R6, R7 = independently C6-30 hydrocarbon contg. 0-4 double bonds; R4 = H, N-acetylglucosaminyl; R5 = (CH2)nMe, n = 0-22; X = spacer group that does not substantially adversely affect the activity or the toxicity of the MDP compd; Y = single bond, peptide residue contg. 1-10 amino acid groups] to a mammal. Another aspect of the invention is directed to methods of treating retroviral infections, such as **HIV** infections by administering an effective amt. of a muramyl dipeptide compd. to a mammal. The invention is also directed to a pharmaceutical compn. for inducing the release of at least one chemokine and treating retroviral infections, such as **HIV** infections, wherein the pharmaceutical compn. includes an amide linked analog of N-Acetylmuramyl-L-Ala-D-Glu-NH2. The invention may further include a method of inducing the release of at least one chemokine and a method of treating retroviral infection in a patient by administering an effective amt. of a non-toxic enterotoxin such as ovine toxic shock syndrome toxin (O-TSST) in combination with the MDP compd. Thus, peptide coupling of muramyl dipeptide Mur(NAc)-L-Ala-D-IsoGln-OH (prepn. given) with L-alanine di(palmitoyloxy)propylamide gave analog II as a white powder after purifn. II and a no. of other analogs were tested for chemokine induction and antiviral activity.

IT **53678-77-6P**

RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of lipophilic muramylpeptide derivs. for treatment of retroviral infection and induction of chemokines)

L62 ANSWER 4 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1997:684420 HCAPLUS
DN 127:345327
TI Non-dendritic backbone peptide carrier
IN Heegaard, Peter Mikael Helweg; Jakobsen, Palle Hoy
PA Pepresearch A/S, Den.; Heegaard, Peter Mikael Helweg; Jakobsen, Palle Hoy
SO PCT Int. Appl., 261 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9738011	A1	19971016	WO 97-DK146	19970403
	W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9725679	A1	19971029	AU 97-25679	19970403
PRAI	DK 96-398		19960403		
	WO 97-DK146		19970403		

AB The present invention relates to a non-dendritic peptide designed for use as a carrier of an immunogenic substance and/or an immune mediator, a construct of said carrier carrying an immunogenic substance and/or an immune mediator, a process for the prepn. of immunogens with high and predictable immunogenicity which comprise said non-dendritic peptide carrier, use of such immunogens for the prodn. of vaccines and vaccines comprising an immunogenic substance and/or an immune mediator on the peptide carrier. The invention also relates to diagnostic or therapeutic embodiments using the non-dendritic peptide carrier, to diagnostic or therapeutic compns. and to methods for the use thereof in diagnosis of diseases and pregnancy as well as in therapy. The non-dendritic peptide carrier according to the invention comprises 10-50 amino acids capable of forming a secondary structure in a benign buffer after liberation from the solid phase.

IT **53678-77-6**, Muramyldipeptide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(non-dendritic backbone peptide carrier for immunogenic peptide, immune mediator or vaccine)

L62 ANSWER 5 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1997:240684 HCAPLUS
DN 126:224271
TI Non-specific vaccination by D-amino-acid containing compounds
IN Slesarev, Vladimir I.; Efimov, Vladimir A.; Oraevsky, Alexander A.; Slesarev, Alexei I.
PA Slesarev, Vladimir I., USA; Efimov, Vladimir A.
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT **Patent**
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9705889	A1	19970220	WO 96-US12525	19960731
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRAI	US 95-510737		19950803		

OS MARPAT 126:224271

AB Non-specific vaccination is achieved by administrating muramyl or glucosaminylmuramyl di- or tri-peptides with D-amino acid residue in a second or third position from the proximal end. The D-amino acid-contg. muramyl or glucosaminylmuramyl di- or tri-peptides are used as supplement to infant formula or human milk to reduce diarrhea, or administered via oral, vaginal, rectal or topic route to reduce cancer or **HIV** transmission through sexual contacts. The presence of N-acetyl-D-glucosaminyl-(1.fwdarw.4)-N-acetylmuramyl-L-alanyl-D-isoglutamine (GMDP) in human milk and yoghurt was detd. by antibody capture assay. Administration of GMDP to prevent Clostridium perfringens-assocd. diarrhea in piglets and inhibition of **HIV** gp120 binding to CD4 receptor by GMDP were also demonstrated. Use of the non-specific anticancer vaccine (GMDP) combined with NMR and ultrasound technol. for its monitoring was also described.

IT **59309-66-9**, N-Acetylmuramyl-L-alanyl-D-glutamine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(D-amino acid-contg. muramyl or glucosaminylmuramyl dipeptide or tripeptide as nonspecific vaccine for redn. of diarrhea, cancer or **HIV** transmission through sexual contact)

L62 ANSWER 6 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1996:731868 HCAPLUS
DN 126:1184
TI MDP derivatives and conjugates having hematopoietic function stimulating activity
IN **Bahr, Georges**; Lefrancier, Pierre; Chedid, Louis
PA **Vacsyn S.A.**, **Fr.**
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT **Patent**
LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9631533	A1	19961010	WO 96-FR527	19960405
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
	FR 2732604	A1	19961011	FR 95-4194	19950407
	FR 2732604	B1	19970606		
	CA 2216599	AA	19961010	CA 96-2216599	19960405
	AU 9655046	A1	19961023	AU 96-55046	19960405
	EP 819136	A1	19980121	EP 96-912079	19960405
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI FR 95-4194 19950407
WO 96-FR527 19960405
OS MARPAT 126:1184
AB A pharmaceutical compn. for stimulating the hematopoietic function and preventing the myelotoxic side-effects of some treatments, contain at least one water-sol. muramyl peptide deriv. such as Muradimetide (I) or muroctasine. I.v. administration of 25 mg I/kg to guinea pigs for 4 days increased the no. of myelocytes from 7x104/mL to 72x104/mL. A soln. of 320 mg 6-O-succinyl-N-acetyl-muramyl-L-alanyl-D-glutamic acid di-Me ester in 10 mL anhyd. DMF was mixed with 0.05 mL of Me morpholine, 0.06 mL of iso-Bu chlorocarbaonate, and 267 mg 3'-azido-3'-deoxythymidine and stirred at 15.degree. for 24 h to obtain 6-O-(succinyl-3'-azido-3'-deoxythymidine)-N-acetyl-muramyl-L-alanyl-D-glutamic acid di-Me ester which was purified (yield:50%).
IT **79787-27-2**
RL: RCT (Reactant)
(MDP derivs. and conjugates having hematopoietic function stimulating activity)

L62 ANSWER 7 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1996:694251 HCAPLUS
DN 125:326402
TI An immunoreactive conjugate, method for its preparation, antibodies to the conjugate and a pharmaceutical composition and diagnostic device containing them
IN Maes, Roland
PA Anda Biologicals S.A., Fr.
SO Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DT **Patent**
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 736770	A2	19961009	EP 96-870042	19960401
	EP 736770	A3	19970502		
	R: BE, DE, FR, GB, IT				
	BE 1009230	A6	19970107	BE 95-316	19950405
	BE 1009917	A6	19971104	BE 96-113	19960208
PRAI	BE 95-316	19950405			
	BE 96-113	19960208			

AB An immunoreactive conjugate is disclosed which contains 1 or more haptens consisting of a sulfhydryl group and one of the following: amino acids, carbohydrates, amino carbohydrates, phosphatidylinositol, sphingosine, and their nitrosyl, acyl, or acetyl derivs., the haptens being coupled to a protein with a mol. wt. >8000 Kd and/or a solid support by a coupling agent capable of binding to the sulfhydryl group of the hapten. Thus, NO-cysteine and NO-N-acetyl-L-cysteine conjugates with albumin were prepd., and birds and mammals were vaccinated. IgG and IgM class antibodies specific for N-acetyl-L-cysteine were detected in the subjects. Addnl. analyses demonstrated that many **HIV**-pos. patients have IgG specific for acetyl-cysteine. Pharmaceutical compns. using these immunoreactive conjugates can be used in the prevention and/or treatment of autoimmunity, **AIDS**, cancer, tuberculosis and a variety of other diseases.
IT **53678-77-6**, N-Acetyl-muramyl-L-alanyl-D-isoglutamine
53678-77-6D, N-Acetyl-muramyl-L-alanyl-D-isoglutamine,

nitrosyl derivs.
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(in prepn. of immunoreactive conjugates with haptens and carrier protein, antibodies to them, and application in diagnosis and treatment of disease)

L62 ANSWER 8 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1996:483722 HCAPLUS
DN 125:140546
TI Induction of cytotoxic T-lymphocyte responses
IN Raychaudhuri, Syamal; Rastetter, William H.
PA Idec Pharmaceuticals Corporation, USA
SO PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9617863	A1	19960613	WO 95-US15433	19951129
	W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5709860	A	19980120	US 94-351001	19941207
	AU 9644104	A1	19960626	AU 96-44104	19951129
	EP 801656	A1	19971022	EP 95-942921	19951129
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	BR 9509872	A	19971125	BR 95-9872	19951129
	NO 9702521	A	19970806	NO 97-2521	19970603
	FI 9702431	A	19970606	FI 97-2431	19970606
PRAI	US 94-351001	19941207			
	US 91-735069	19910725			
	US 92-919787	19920724			
	WO 95-US15433	19951129			

AB Methods and compns. useful for inducing a cytotoxic T-lymphocyte response (CTL) in a human or domesticated or agriculturally important animal. The method includes the steps of providing the antigen to which the CTL response is desired and providing an antigen formulation which comprises, consists, or consists essentially of two or more of a stabilizing detergent, a micelle-forming agent, and an oil. This antigen formulation is preferably lacking in an immunostimulating peptide component, or has sufficiently low levels of such a component that the desired CTL response is not diminished. This formulation is provided as a stable oil-in-water emulsion.
IT **53678-77-6**, Muramyl dipeptide
RL: MOA (Modifier or additive use); USES (Uses)
(compn. contg. antigen and detergent and micelle-forming agent and oil for induction of cytotoxic T lymphocyte)

L62 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1996:440899 HCAPLUS
DN 125:96040

TI Immunogenic compositions solubilised in a hydrophobic solvent
IN New, Roger Randal Charles
PA Cortecs Limited, UK
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9614871	A1	19960523	WO 95-GB2675	19951114
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2205083	AA	19960523	CA 95-2205083	19951114
AU 9538534	A1	19960606	AU 95-38534	19951114
EP 792165	A1	19970903	EP 95-936690	19951114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10508834	T2	19980902	JP 95-515847	19951114
FI 9702054	A	19970514	FI 97-2054	19970514
NO 9702219	A	19970711	NO 97-2219	19970514
PRAI GB 94-22990		19941115		
WO 95-GB2675		19951114		

AB An immunogenic compn. comprising an immunogen solubilised, or otherwise distributed, in a hydrophobic solvent in the absence of a hydrophilic phase. Preferably, the immunogenic compn. is provided as an oral vaccine. Thus, 40 .mu.L of tetanus toxoid (5 mg/mL) was added to 1 mL dispersion of 100 mg/mL soya phosphatidyl choline and the mixt. was lyophilized overnight, followed by addn. of 1 mL of oleic acid to obtain a crystal clear soln. Mice were administered 100 .mu.L of above soln. either s.c. or through an intragastric tube. Antibody levels against tetanus antigen after two wk was much more than controls.
IT **53678-77-6**, Muramyldipeptide
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(immunogenic compns. solubilised in a hydrophobic solvent)

L62 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1996:369794 HCAPLUS
DN 125:26240
TI Muramyl peptide compositions for inhibiting **HIV** replication
IN **Bahr, Georges**
PA **Vacsyn S.A.**, **Fr.**
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT **Patent**
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9609837	A1	19960404	WO 95-FR1239	19950926

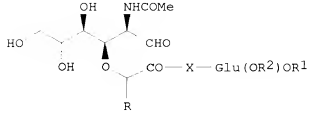
LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

FR 2715305	A1	19950728	FR 94-786	19940125	
FR 2715305	B1	19960315			
CA 2181899	AA	19950727	CA 95-2181899	19950124	
AU 9515809	A1	19950808	AU 95-15809	19950124	
EP 741573	A1	19961113	EP 95-907694	19950124	

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

JP 09509409	T2	19970922	JP 95-519390	19950124	

PRAI FR 94-786 19940125
WO 95-FR77 19950124
OS MARPAT 123:276025
GI



I

AB An externally active immunostimulating pharmaceutical compn. is disclosed which contains a diester I (R = Me,;X = L-Ala, L-Thr; R1 = C1-4 hydrocarbyl; R2 = C1-2 hydrocarbyl) in an externally administered formulation compatible with an administration of active principle of 0.1-5 mg/kg to humans or animals. The immunostimulant is e.g. muradimetide. The activity of muradimetide (e.g. adjuvant activity, antibacterial activity) was detd.

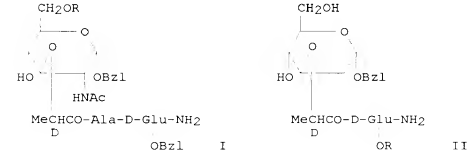
IT **53678-77-6 59366-95-9 60355-78-4 63555-62-4 74817-61-1 90159-44-7 92512-64-6**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(muramyl peptide diesters in oral form as immunostimulating agents)

IT **60355-79-5**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(muramyl peptide diesters in oral form as immunostimulating agents)

L62 ANSWER 12 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1995:538414 HCAPLUS
DN 122:274059
TI Hydrogel-microencapsulated vaccines
IN Andrianov, Alexander K.; Jenkins, Sharon A.; Payne, Lendon G.; Roberts, Bryan E.
PA Virus Research Institute, USA
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DT **Patent**
LA English

CODEN: CEXIAL; ISSN: 0009-9104
PB Blackwell
DT Journal
LA English
AB Since the identification of the **HIV** virus, important advances have been achieved in the definition of potential subunit vaccines. The authors investigated the immunogenicity of a recombinant gp160 antigen and of two gp41 peptides from **HIV**-1LAI assocd. with 7 different adjuvant formulations in squirrel monkeys. All animals were immunized twice with gp160 and then with a gp41 peptide using the same formulation. All adjuvants used led to a subsequent antibody response against gp160, and 55% of the animals immunized developed anti-gp160 antibodies that could neutralize the virus in vitro. Specific anti-gp41 antibody response was also obsd. Results obtained underlined the key role of the adjuvant formulation in the antibody response against a given part of the immunogen, and indicate that such immunogenicity-related investigation can be carried out conveniently in the squirrel monkey Saimiri sciureus.
IT **53678-77-6**, Muramyl dipeptide
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunogenicity of **HIV**-1 gp160 and env peptides in squirrel monkey Saimiri sciureus using alumina and exptl. adjuvants)

L64 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 1998 ACS
AN 1995:21229 HCAPLUS
DN 122:81977
TI A new class of antitumor agents: conjugates of MDP and acridine/acridone derivatives
AU Kolodziejczyk, A. M.; Dzierzbicka, K.; Kolodziejczyk, A. S.
CS Dep. Org. Chem., Tech. Univ. Gdansk, Gdansk, PL 80-952, Pol.
SO Pol. J. Chem. (1994), 68 1023-9
CODEN: PJCHDQ; ISSN: 0137-5083
DT Journal
LA English
GI



AB The synthesis of title muramyl dipeptide (MDP) conjugates I (R = acridine or acridone derivs.) and II has been described. In conjugates I, the hydroxyl group at C6 of the muramyl moiety was

acylated with acridine carboxy derivs., whereas conjugates II were formed by esterification of isoglutamine carboxyl group with hydroxy derivs. of acridine. The results of the antitumor and anti-**HIV** assays for some of the conjugates are also presented.

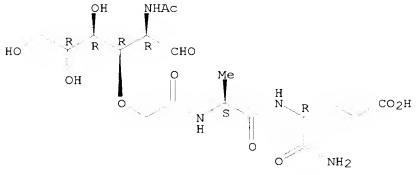
IT **53678-77-6DP**, Muramyl dipeptide, acridine/acridone conjugates
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of muramyl dipeptide conjugates with acridine/acridone derivs. as antitumor agents)

L64 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 1998 ACS
AN 1994:603135 HCAPLUS
DN 121:203135
TI Anti-**HIV** and anticancer activity of MDP and acridine derivative conjugates
AU Dzierzbicka, Krystyna; Kolodziejczyk, Aleksander M.; Sosnowska, Danuta; Mysliwski, Andrzej
CS Dep. Organic Chemistry, Technical Univ. of Gdansk, Gdansk, PL-80-952, Pol.
SO Pept. 1992, Proc. Eur. Pept. Symp., 22nd (1993), Meeting Date 1992, 889-90. Editor(s): Schneider, Conrad H.; Eberle, Alex N. Publisher: ESCOM, Leiden, Neth.
CODEN: 60LUAN
DT Conference
LA English
AB Taking into account both the immunostimulatory and synergistic properties of muramyl dipeptide (MDP) and anticancer potency of acridine/acridone derivs., the authors decided to conjugate these compds. covalently. Resulting conjugates exhibit substantial anticancer and anti-**HIV** activities and their toxicity is considerably reduced compared to the acridine counterparts.
IT **53678-77-6D**, Muramyl dipeptide, conjugates with acridine derivs.
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-**HIV** and anticancer activity of)

L64 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 1998 ACS
AN 1994:577166 HCAPLUS
DN 121:177166
TI Efficacy of inactivated whole **HIV**-2 vaccines with various adjuvants in cynomolgus monkeys
AU Putkonen, Per; Nilsson, Charlotta; Walther, Lilian; Ghavamzadeh, Lili; Hild, Kerstin; Broliden, Kristina; Biberfeld, Gunnel; Thorstensson, Rigmor
CS Department Immunology, Swedish Institute Infectious Disease Control, Stockholm, Swed.
SO J. Med. Primatol. (1994), 23(2-3), 89-94
CODEN: JMPMAO; ISSN: 0047-2565
DT Journal
LA English
AB Twenty-one cynomolgus monkeys were immunized with whole inactivated **HIV**-2 prepns. administered with various adjuvants (incomplete Freund's adjuvant, Alum, Ribi, MDP, or Iscoms) and challenged with 10 or 100 MID50 of a homologous monkey-cell grown, cell-free **HIV**-2.. Seven animals were completely protected against infection, three showed reduced virus replication. The vaccines elicited neutralizing and ADCC antibodies; the titers did

L67 ANSWER 1 OF 1 REGISTRY COPYRIGHT 1998 ACS
RN **61136-12-7** REGISTRY
CN D-.alpha.-Glutamine, N-(N-acetylnormuramoyl)-L-alanyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN D-.alpha.-Glutamine, N2-[N-(N-acetylnormuramoyl)-L-alanyl]-
OTHER NAMES:
CN Almurtide
CN CGP 11637
CN Desmethylmuramyldipeptide
CN N-Acetyldesmethylmuramyl-L-alanyl-D-isoglutamine
CN N-Acetylnormuramyl-L-alanyl-D-isoglutamine
FS STEREOSEARCH
DR 98725-10-1, 68426-50-6, 72768-58-2, 84227-98-5, 87349-50-6
MF C18 H30 N4 O11
CI COM
LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAPLUS, CASREACT, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



74 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
74 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:301384

REFERENCE 2: 128:304812

REFERENCE 3: 122:161318

REFERENCE 4: 121:18008

REFERENCE 5: 120:267865

REFERENCE 6: 118:167134

REFERENCE 7: 118:57798

REFERENCE 8: 118:16298

DT Journal
FS 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Studies indicate that adjuvant formulations based on liposomes, nontoxic lipid A, and muramyl peptide derivatives are safe and effective for vaccine use. Future research on the immunobiology of these adjuvants as well as the mechanisms by which adjuvants can alter the quality of immune responses may play an important role in determining their efficacy in malaria vaccines.
CT EMTAGS: infection (0310); therapy (0160); prevention (0165); mammal (0738); human (0888); nonhuman (0777); human experiment (0104); oral drug administration (0181); subcutaneous drug administration (0183); intramuscular drug administration (0184); intravenous drug administration (0182); intradermal drug administration (0176); conference paper (0061); adverse drug reaction (0198); iatrogenic disease (0300)
Medical Descriptors:
*malaria: DT, drug therapy
*malaria: PC, prevention
*vaccination
*immunobiology
drug formulation
drug design
immunogenicity
drug safety
drug activity
drug efficacy
antibody response
drug tolerance
side effect
human
nonhuman
clinical trial
phase 1 clinical trial
oral drug administration
subcutaneous drug administration
intramuscular drug administration
intravenous drug administration
intradermal drug administration
conference paper
Drug Descriptors:
*malaria vaccine: CT, clinical trial
*malaria vaccine: DT, drug therapy
*malaria vaccine: PR, pharmaceutics
*immunological adjuvant: PR, pharmaceutics
*liposome: PR, pharmaceutics
*muramyl dipeptide derivative: PR, pharmaceutics
*lipid a: PR, pharmaceutics
aluminum potassium sulfate: PR, pharmaceutics
phosphoryl lipid a: AE, adverse drug reaction
phosphoryl lipid a: CT, clinical trial
phosphoryl lipid a: TO, drug toxicity
phosphoryl lipid a: PR, pharmaceutics
lipid a derivative: TO, drug toxicity
lipid a derivative: PR, pharmaceutics

saponin: PR, pharmaceutics
iscom: PR, pharmaceutics
murabutide: PR, pharmaceutics
muroctasin: PR, pharmaceutics
n acetylmuramylalanyl dextro isoglutaminylalanyl dipalmitoylphosphatidylethanolamine: PR, pharmaceutics
squalene: PR, pharmaceutics
bacterium lipopolysaccharide: TO, drug toxicity
bacterium lipopolysaccharide: PR, pharmaceutics
glucosamine derivative: TO, drug toxicity
glucosamine derivative: PR, pharmaceutics
sporozoite vaccine: AE, adverse drug reaction
sporozoite vaccine: CT, clinical trial
sporozoite vaccine: PR, pharmaceutics
cell wall skeleton: PR, pharmaceutics
freund adjuvant: PR, pharmaceutics
membrane antigen
cord factor: PR, pharmaceutics
hepatitis a vaccine: PR, pharmaceutics
influenza vaccine: PR, pharmaceutics
tetanus toxoid: AE, adverse drug reaction
tetanus toxoid: PR, pharmaceutics
bacterial protein: AE, adverse drug reaction
bacterial protein: PR, pharmaceutics
human immunodeficiency virus vaccine: PR, pharmaceutics
unindexed drug
merozoite surface antigen 1: PR, pharmaceutics
rhoptry associated protein 1: PR, pharmaceutics
serine repeat antigen: PR, pharmaceutics

RN 95991-05-2; 10043-67-1; 88598-53-2; 8047-15-2; **74817-61-1**; 78113-36-7; 83461-56-7; 111-02-4; 7683-64-9; 9007-81-2; 61512-20-7; 93384-51-1
CN (1) Mf 59; (2) Detox
CO (1) Ciba geigy (Switzerland); (2) Ribi (United States)

=> fil aidsline

FILE 'AIDSLINE' ENTERED AT 09:21:10 ON 08 DEC 1998

FILE COVERS 1980 TO 25 NOV 1998 (19981125/ED)

Aidsline has been reloaded with 1998 MeSH headings. See HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot l76

L76 ANSWER 1 OF 38 AIDSLINE
AN 1998:17871 AIDSLINE
DN ICA12-98392561
TI Inhibition of HIV-1 replication in reservoir cells by the safe immunomodulator **Murabutide**.
AU Bahr G; Darcissac E; Grau O; Truong M J; Dewulf J; Debard C; Capron A
CS Institut Pasteur de Lille, INSERM U167, France.
SO Int Conf AIDS, (1998). Vol. 12, pp. 349 (Abstract No. 22424).

CY Switzerland
DT Abstract
FS ICA12
LA English
EM 199812
AB OBJECTIVES: To assess the efficacy of the clinically-acceptable immunomodulator **Murabutide**, a butyl ester derivative of MDP, on the inhibition of HIV replication in monocyte-derived macrophages (MDM) and dendritic cells (MDDC). METHODS: Acutely infected MDMs and MDDCs with M-tropic HIV-1 isolates, were maintained in the absence or presence of **Murabutide**. Reverse transcriptase (RT) or P24 levels in culture supernatants were evaluated 7-21 days post-infection. Proviral DNA and viral mRNA were quantified in infected cells using polymerase chain reaction (PCR) and RT-PCR respectively. The levels of secreted cytokines were also tested by specific ELISA kits. RESULTS: Addition of **Murabutide** to infected MDMs and DCs resulted in 60-100% inhibition of viral replication in cultures from 10 different donors. This effect was found to be mediated, in part, by the induction of high levels of HIV-suppressing beta chemokines, MIP-1 alpha, MIP-1 beta and RANTES. In addition, cells stimulated with **Murabutide** immediately after infection presented highly reduced levels of proviral DNA at the 24 hour period. Analysis of the levels of unspliced and singly-spliced viral mRNA in 8-12 days infected cells showed over 90% inhibition of viral transcripts in **Murabutide**-treated cultures. This inhibitory effect of **Murabutide** was also evident in reservoir cells acutely infected with primary HIV-1 isolates. The safe synthetic immunomodulator **Murabutide** exerts potent HIV-suppressing activity in reservoir cells and is currently being evaluated as an adjunct to antiretroviral therapy.
CT Check Tags: Human
***Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives**
Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology
*Adjuvants, Immunologic: PD, pharmacology
Cells, Cultured
*Dendritic Cells: VI, virology
*HIV Infections: DT, drug therapy
*HIV Infections: IM, immunology
HIV Infections: VI, virology
*HIV-1: DE, drug effects
*HIV-1: PH, physiology
*Macrophages: VI, virology
Virus Replication: DE, drug effects
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine); 74817-61-1 (N-acetylmuramyl-alanylglutamine-n-butyl ester)**
CN 0 (Adjuvants, Immunologic)

L76 ANSWER 2 OF 38 AIDSLINE
AN 1998:9001 AIDSLINE
DN MED-98234020
TI Involvement of T cells in enhanced resistance to Klebsiella pneumoniae septicemia in mice treated with liposome-encapsulated muramyl tripeptide phosphatidylethanolamine or gamma interferon.
AU ten Hagen T L; van Vianen W; Savelkoul H F; Heremans H; Buurman W A; Bakker-Woudenberg I A
CS Department of Clinical Microbiology and Antimicrobial Therapy, Erasmus University Rotterdam, The Netherlands.

tenhagen@heel.fgg.eur.nl
SO INFECTION AND IMMUNITY, (1998). Vol. 66, No. 5, pp. 1962-7.
Journal code: GO7. ISSN: 0019-9567.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals; Cancer Journals
LA English
OS MEDLINE 98234020
EM 199807
AB We have previously shown that prophylactic administration of the liposome-encapsulated immunomodulating agents muramyl tripeptide phosphatidylethanolamine (MTPPE) and gamma interferon (IFN-gamma) results in strongly increased survival of mice from a normally lethal septicemia with Klebsiella pneumoniae. It was anticipated that the treatment acts on macrophages and nonspecifically augments host resistance to various infections. In the present study, we provide evidence for a key role for T cells in host defense potentiation by the liposomal immunomodulators toward K. pneumoniae septicemia. It is shown that both CD4 and CD8 cells are important in immunomodulation, most likely due to production of IFN-gamma. Depletion of circulating IFN-gamma resulted in strong reduction of the antimicrobial host defense activation. Administration of interleukin-10 resulted in decreased antimicrobial host defense activation by liposomal immunomodulators. Moreover, administration of liposomal immunomodulators was shown to induce predominantly T-helper type 1 (Th1) cell populations in the spleen. These findings indicate that immunomodulation with liposomal MTPPE and IFN-gamma favors Th1 and NK cell activation.
CT Check Tags: Animal; Female; Support, Non-U.S. Gov't
***Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives**
Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage
*Adjuvants, Immunologic: AD, administration & dosage
*Bacteremia: IM, immunology
Histocompatibility Antigens Class II: AN, analysis
*Interferon Type II: AD, administration & dosage
Interleukin-10: PD, pharmacology
*Klebsiella pneumoniae
*Klebsiella Infections: IM, immunology
Liposomes
Mice
Mice, Inbred C57BL
*Phosphatidylethanolamines: AD, administration & dosage
*T-Lymphocytes: IM, immunology
Th1 Cells: IM, immunology
Th2 Cells: IM, immunology
RN 130068-27-8 (Interleukin-10); **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 82115-62-6 (Interferon Type II); 83461-56-7 (CGP 19835 A)
CN 0 (Adjuvants, Immunologic); 0 (Histocompatibility Antigens Class II); 0 (Liposomes); 0 (Phosphatidylethanolamines)

L76 ANSWER 3 OF 38 AIDSLINE
AN 1997:23069 AIDSLINE
DN MED-97448354
TI Study of the adjuvant activity of new MDP derivatives and purified saponins and their influence on HIV-1 replication in vitro.
AU Krivorutchenko Y L; Andronovskaja I B; Hinkula J; Krivoshein Y S;

CT Check Tags: Animal; Female; In Vitro
***Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives**
Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage
*Adjuvants, Immunologic: AD, administration & dosage
*Antigens: AD, administration & dosage
*Cytotoxicity, Immunologic
*CD8-Positive T-Lymphocytes: IM, immunology
Immunization
Mice
Mice, Inbred C57BL
Ovalbumin: IM, immunology
Solubility
Tumor Cells, Cultured
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 70280-03-4 (N-acetyl-beta-glucosaminyl-N-acetylmuramyl-alanylisoglutamine); 9006-59-1 (Ovalbumin)
CN 0 (Adjuvants, Immunologic); 0 (Antigens)

L76 ANSWER 6 OF 38 AIDSLINE
AN 1996:436 AIDSLINE
DN MED-96020392
TI Alteration of spleen lymphocyte populations in rats with arthritis induced by muramyl dipeptide analogue or complete adjuvant.
AU Sugawara T; Miyamoto M; Takada S; Nomura M; Kato M
CS Drug Safety Research Center, Daiichi Pharmaceutical Co., Ltd., Tokyo, Japan.
SO INTERNATIONAL JOURNAL OF TISSUE REACTIONS, (1995). Vol. 17, No. 1, pp. 5-13.
Journal code: GTG. ISSN: 0250-0868.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 96020392
EM 199603
AB To examine the involvement of lymphocytes in the development of MDP-Lys(L18)-induced arthritis (MIA) in rats and the exacerbation of MIA by cyclosporin A (CsA), we analysed the spleen lymphocyte subset using monoclonal antibodies and flow cytometry during the development of arthritis and compared the results with those found in adjuvant-induced arthritis (AIA). Subcutaneous injection of MDP-Lys(L18) 4 mg/kg to male Lewis rats for 14 days caused very slight and quite clear increases in tarsal joint thickness on days 8 and 15, respectively. This increase was significantly enhanced by co-administration of CsA 10 mg/kg on both of these days. Adjuvant intracutaneously injected once increased the thickness only on day 15, and this was completely inhibited by CsA. The populations of CD4+ and CD8+ cells were increased and decreased, respectively, increasing the CD4+/CD8+ ratio, from day 8 in MIA. CsA enhanced the MDP-Lys(L18)-induced changes in these populations and caused additional decreases in the number of CD5+ cells. Only the CD4+ cell population was increased on day 15 in AIA, and this increase was inhibited by CsA. These results suggest that the spleen lymphocyte subsets in MIA have a different role from those in AIA, and that the contribution of enhancement of the subset changes to the exacerbating effect of CsA on MIA.
CT Check Tags: Animal; Male

*Squalene: AD, administration & dosage
Vaccines, Synthetic: AD, administration & dosage
*Vaccines, Synthetic: IM, immunology
RN 111-02-4 (Squalene); **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 83461-56-7 (CGP 19835 A)
CN 0 (Adjuvants, Immunologic); 0 (AIDS Vaccines); 0 (HIV Antibodies); 0 (HIV Envelope Protein gp120); 0 (MF59 oil emulsion); 0 (Phosphatidylethanolamines); 0 (Polysorbates); 0 (Vaccines, Synthetic)

L76 ANSWER 9 OF 38 AIDSLINE
AN 1994:8699 AIDSLINE
DN MED-94293161
TI Effect of MTP-PE liposomes and interleukin-7 on induction of antibody and cell-mediated immune responses to a recombinant HIV-envelope protein.
AU Bui T; Dykers T; Hu S L; Faltynek C R; Ho R J
CS Department of Pharmaceutics, University of Washington, Seattle 98195.
NC AI 31854 (NIAID)
SO JOURNAL OF ACQUIRED IMMUNE DEFICIENCY SYNDROMES, (1994). Vol. 7, No. 8, pp. 799-806.
Journal code: JOF. ISSN: 0894-9255.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 94293161
EM 199410
AB We investigated the ability of human recombinant interleukin-7 (IL-7) to enhance the immune responses of mice vaccinated with either the alum-associated or liposome-formulated recombinant human immunodeficiency virus (HIV)-envelope protein, env-2-3SF2 (a nonglycosylated denatured gp 120 of HIV-1SF2 produced in genetically engineered yeast). Pathogen-free (C3H) mice were vaccinated on days 0, 14, and 28 with 10 micrograms of either the alum-associated env-2-3SF2 or liposome-formulated env-2-3SF2, both containing a lipophylic muramyl tripeptide, MTP-PE. Liposome-formulated IL-7 (5 micrograms/mouse) or empty liposomes were given on days 7, 14, 21, and 28. Antibody response against the immunized antigen, evaluated on day 21 and day 35 or 42, showed that liposome-formulated antigen induced higher antibody titer than did alum-associated antigen, and these antibody responses can be enhanced by concurrent administration of IL-7 liposomes. Spleen cells were harvested on day 21 and day 35 or 42 to evaluate cytotoxic T lymphocyte responses directed against autologous cells infected with vaccinia virus-expressing HIV-envelope protein. Mice treated with liposome-formulated antigen expressed the highest cytotoxic t-lymphocyte (CTL) activity, regardless of whether IL-7 liposome was given as an immune potentiator. In contrast, spleen cells from mice vaccinated with alum-associated antigen exhibited minimal CTL response, which was enhanced by concurrent IL-7 liposome treatment. Collectively, IL-7 liposome treatment enhanced the antibody production of the alum-associated or liposome-formulated env-2-3SF2, whereas its enhancement of CTL activity was detected only in mice vaccinated with alum-associated antigen.
CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
***Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives**

+ FA). All of the monkeys became infected after intravenous challenge. However, 16 days following infection, viral antigenemia was reduced in both groups of vaccinates compared to controls. After 23 days antigenemia in the gp110 + SAF-M group remained at the same level as on day 16, whereas antigenemia in the gp140 + FA group was significantly reduced further than the level observed on day 16. Both vaccines induced blastogenic responses in PBMC cultures stimulated with rgp140, which decreased after repeated immunizations. Both vaccines induced high ELISA titers of IgG antibody against rgp140 that were equivalent to the titers in asymptomatic long-term survivors (LTSs). gp110 +/- SAF-M induced high titers of neutralizing antibody. In contrast, gp140 + FA failed to induce neutralizing antibody, suggesting that the natural conformation of the antigen may be essential for the induction of neutralizing antibody. High titers of antibodies capable of complement-mediated cytolysis (ACC) were induced by gp110 + SAF-M, whereas minimal ACC antibodies were induced by gp140 + FA. In spite of high titers of antibodies by ELISA, neither gp110 + SAF-M nor gp140 + FA vaccines induced detectable levels of antibody capable of antibody dependent cell-mediated cytolysis (ADCC). Detectable amounts of MHC class I-restricted, CD8+ cytotoxic T lymphocytes (CTLs) were not induced in immunized monkeys before challenge. After challenge and infection, antibody responses to glycoprotein (detected by ELISA and ACC) as well as glycoprotein-specific CTLs were induced in gp140 + FA vaccinates at levels higher than in nonimmunized control animals, indicating a priming effect by gp140 + FA immunization. No priming effect for ADCC antibody induction was observed in monkeys vaccinated with either gp110 + SAF-M or gp140 + FA. Rhesus monkey groups immunized with two different SIV envelope vaccines differed regarding potentially protective humoral and cell-mediated immune responses. The physical state of the immunogens, the type of adjuvant used, and/or the immunization protocol apparently affected these responses in both a qualitative and quantitative manner.

CT Check Tags: Animal; Human; Support, U.S. Gov't, P.H.S.
Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives
Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage
Antibodies, Viral: BI, biosynthesis
*AIDS Vaccines: IM, immunology
Cells, Cultured
Disease Models, Animal
Enzyme-Linked Immunosorbent Assay
Freund's Adjuvant: IM, immunology
IgG: IM, immunology
Macaca mulatta
Neutralization Tests
Polysorbates: AD, administration & dosage
Retroviridae Proteins: IM, immunology
*Simian Acquired Immunodeficiency Syndrome: IM, immunology
Simian Acquired Immunodeficiency Syndrome: PC, prevention & control
Squalene: AA, analogs & derivatives
Squalene: AD, administration & dosage
T-Lymphocytes, Cytotoxic: IM, immunology
Vaccines, Synthetic: IM, immunology
Viral Envelope Proteins: IM, immunology

RN 111-02-4 (Squalene); **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 9007-81-2 (Freund's Adjuvant)

WS-B27-2).
CY GERMANY: Germany, Federal Republic of
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Abstract
(RANDOMIZED CONTROLLED TRIAL)
FS ICA9
LA English
EM 199311
AB A phase 1 randomized double-blind study was performed to determine safety and immunogenicity in HIV-seronegative adults of three injections (at day 0 and months 1 and 6) of a vaccine composed of 25 micrograms of recombinant HIV gp 120 (SF-2) antigen combined with MF-59 emulsion containing a muramyl tripeptide (MTP-PE) in a dose escalation format. Forty-two healthy HIV-seronegative adults, with normal laboratory studies were vaccinated. Each vaccine contained MF59 emulsion and each subject received MTP-PE (micrograms per injection) dosing as follows: Group 1 (0/0/0); Group (1/1/1); Group 2 (10/10/10); Group 4 (50/50/50); Group 5 (10/0/0); Group 6 (100/0/0). Two subjects in each group were randomized to receive placebo-antigen while 6 received gp 120. All subjects, except one, received all three immunization. Injections were, in general, well tolerated. ELISA antibodies directed to gp 120 developed in the expected number of subjects. All subjects developing ELISA antibodies also developed neutralizing titers to SF-2 comparable to titers observed in naturally infected subjects. Virus neutralizing to a heterologous strain (MN) has also been observed. Durability of antibody responses has been documented 6 months following the third immunization in the first three groups. Lymphocyte proliferation data has been documented in subjects developing gp120 antibody and has also demonstrated durability over the study period.
CT Check Tags: Human
***Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives**
Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
*Adjuvants, Immunologic
Adult
*AIDS Vaccines
AIDS Vaccines: AD, administration & dosage
AIDS Vaccines: IM, immunology
Dose-Response Relationship, Immunologic
Double-Blind Method
Emulsions
HIV Antibodies: BI, biosynthesis
HIV Envelope Protein gp120: AD, administration & dosage
*HIV Envelope Protein gp120: IM, immunology
*HIV-1: IM, immunology
Neutralization Tests
*Phosphatidylethanolamines: IM, immunology
Recombinant Proteins: AD, administration & dosage
Recombinant Proteins: IM, immunology
Safety
Vaccines, Synthetic: AD, administration & dosage
Vaccines, Synthetic: IM, immunology
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 83461-56-7 (CGP 19835 A)
CN 0 (Adjuvants, Immunologic); 0 (AIDS Vaccines); 0 (Emulsions); 0 (HIV Antibodies); 0 (HIV Envelope Protein gp120); 0 (Phosphatidylethanolamines); 0 (Recombinant Proteins); 0 (Vaccines,

Synthetic)

L76 ANSWER 13 OF 38 AIDSLINE
AN 1993:12524 AIDSLINE
DN ICA9-93335769
TI A phase I HIV-1 vaccine trial in asymptomatic HIV-infected individuals using Env 2-3 in MF-59 with or without MTP-PE. NIAID AVEG.
AU Corey L; McElrath J; Keefer M; Paxton W; Sposto R; Chernoff D
CS Univ of Washington, Seattle.
SO Int Conf AIDS, (1993). Vol. 9, No. 1, pp. 494 (Abstract No. PO-B28-2152).
CY GERMANY: Germany, Federal Republic of
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Abstract
(RANDOMIZED CONTROLLED TRIAL)
FS ICA9
LA English
EM 199311
AB OBJECTIVES: To evaluate the safety and virologic responses in asymptomatic HIV-infected individuals following immunization with a gp120 subunit HIV-1SF-2 vaccine and MTP-PE adjuvant in a randomized, blinded, controlled trial. METHODS: Asymptomatic HIV-1-infected persons lacking plasma viremia with CD4 counts > 600 cells/ul (Group A, N = 30) or 400-550 cells/ul (Group B, N = 15) were immunized with either Env 2-3 (30 micrograms) in MF59 100 micrograms MTG-PE or MF59 100 micrograms MTP-PE at months 0, 1, and 4. Immunizations at months 7 and 10 are in progress. Serial measurements of CD4 cell count, quantitative PBMC viral culture, plasma virus culture, PBMC DNA PCR, and plasma RNA PCR were made. RESULTS: The vaccine was associated with both local pain and systemic symptoms in 82% and 40% of recipients, respectively. All symptoms resolved within 48-72 hours, and no volunteer refused further vaccination as a result of these symptoms. To date, no statistically significant differences in CD4 cell count and quantitative PBMC culture have been seen in the treatment vs control groups. Analysis of the frequency of plasma viremia, quantitative PBMC DNA PCR, and quantitative plasma RNA PCR data are in progress; preliminary analysis suggest a trend in one of the vaccine groups. CONCLUSIONS: The Env 2-3 vaccine in MF59 MTP-PE was safe, and was not associated with a discernable increase in HIV replication. At present, no detectable alterations in CD4 cell counts or in quantitative PBMC viral culture have been found between vaccine-treated or untreated subjects. However, complete analysis of the quantitative PCR data are pending.
CT Check Tags: Human
Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives
Adjuvants, Immunologic
*AIDS Vaccines: TU, therapeutic use
Double-Blind Method
DNA, Viral: BL, blood
*HIV Envelope Protein gp120: IM, immunology
HIV Infections: BL, blood
HIV Infections: MI, microbiology
*HIV Infections: TH, therapy
*HIV-1: IM, immunology
HIV-1: IP, isolation & purification
Phosphatidylethanolamines

Polymerase Chain Reaction
Proviruses: IP, isolation & purification
Recombinant Proteins: IM, immunology
RNA, Viral: BL, blood
Safety
Vaccines, Synthetic: IM, immunology
Viremia: BL, blood
Viremia: MI, microbiology
*Viremia: TH, therapy
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 83461-56-7 (CGP 19835 A)
CN 0 (Adjuvants, Immunologic); 0 (AIDS Vaccines); 0 (DNA, Viral); 0 (HIV Envelope Protein gp120); 0 (Phosphatidylethanolamines); 0 (Recombinant Proteins); 0 (RNA, Viral); 0 (Vaccines, Synthetic)

L76 ANSWER 14 OF 38 AIDSLINE
AN 1993:11206 AIDSLINE
DN ICA9-93334177
TI Phase I trial of native HIV-1SF-2 rgp120 candidate vaccine. NIAID AIDS Vaccine Clinical Trials Network.
AU Graham B; Keefer M; McElrath J; Matthews T; Schwartz D; Gorse G; Sposto R; Chernoff D
CS Vanderbilt Univ., Nashville, TN.
SO Int Conf AIDS, (1993). Vol. 9, No. 1, pp. 250 (Abstract No. PO-A29-0692).
CY GERMANY: Germany, Federal Republic of
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Abstract
(RANDOMIZED CONTROLLED TRIAL)
FS ICA9
LA English
EM 199311
AB OBJECTIVES: To evaluate the safety and immunogenicity of rgp120 from HIV-1SF-2 in MF59 emulsion formulated with or without MTP-PE (Biocine, Emeryville, CA). METHODS: Healthy, HIV-seronegative, low risk adult volunteers were immunized at 0, 1, and 6 months with 15 micrograms or 50 micrograms of rgp120 in MF59 with or without 50 micrograms of MTP-PE. Another group of healthy adult women received 5 monthly injections of MF59 alone or 50 micrograms rgp120 in MF59. The studies were randomized and double-blind. Clinical responses and laboratory toxicities were monitored and immune responses were analyzed. RESULTS: 12/48 volunteers had significant erythema or induration at the site of vaccination; 9/12 received MTP-PE. All 4 with significant local pain and tenderness received MTP-PE as did 7/9 with significant fever, malaise, or headache. Serologic data 1 month after the third dose is presented below as mean O.D. or titer among responders and fraction of responders. V3 = peptide ELISA; NT = neutralization; FI = fusion inhibition. TABULAR DATA, SEE ABSTRACT VOLUME. CONCLUSIONS: The Biocine HIV-1SF-2 native rgp120 product is safe and immunogenic. MTP-PE increases local and systemic side effects, and has no significant adjuvant effect for humoral responses beyond that afforded by MF59. Three injections of 50 micrograms rgp120 induced type-specific functional antibody responses in 19/21 vaccinees tested to date.
CT Check Tags: Comparative Study; Female; Human
Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives
Acetylmuramyl-Alanyl-Isoglutamine: AD, administration &

currently being examined in animal and human trials for their suitability as adjuvants in potential vaccines against acquired immunodeficiency syndrome (AIDS). It may prove to be beneficial to select adjuvants that do not induce NF-kappa B activation and particularly if the vaccines are to be aimed at seropositive individuals. We have examined a battery of synthetic immunostimulants of the muramyl peptide family for their ability to activate NF-kappa B in human and mouse cell lines. In this report, we demonstrate selective activation of NF-kappa B in different cell lines and by different muramyl peptides possessing immunostimulatory activities. The mechanism of such activation is apparently via production of reactive oxygen intermediates (ROI) since pretreatment of cells with antioxidants blocked subsequent activation of NF-kappa B. However, among all the molecules tested only one lipophilic, non-pyrogenic adjuvant active muramyl peptide showed a complete lack of NF-kappa B activation in all cell lines tested. This molecule could well become the adjuvant of choice in future AIDS vaccines.

CT Check Tags: Animal; Human; In Vitro
Acetylmuramyl-Alanyl-Isoglutamine: CH, chemistry
***Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology**
*Acquired Immunodeficiency Syndrome: TH, therapy
*Adjuvants, Immunologic
Antioxidants: PD, pharmacology
Base Sequence
Cell Line
Gene Expression
Interleukin-8: GE, genetics
Mice
Molecular Sequence Data
*NF-kappa B: ME, metabolism
Oligodeoxyribonucleotides: CH, chemistry
Reactive Oxygen Species: ME, metabolism
Structure-Activity Relationship
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**
CN 0 (Adjuvants, Immunologic); 0 (Antioxidants); 0 (Interleukin-8); 0 (NF-kappa B); 0 (Oligodeoxyribonucleotides); 0 (Reactive Oxygen Species)

L76 ANSWER 20 OF 38 AIDSLINE
AN 1992:11415 AIDSLINE
DN ICA8-92400540
TI Purified inactivated SIV vaccine: comparison of adjuvants.
AU Vaslin B; Le Grand R; Vogt G; Roques P; Stoeckel P; Salk J; Dormont D
CS CRSSA/CEA, Fontenay aux Roses, France.
SO Int Conf AIDS, (1992). Vol. 8, No. 2, pp. A42 (Abstract No. PoA 2239).
CY Netherlands
DT Abstract
FS ICA8
LA English
EM 199212
AB OBJECTIVE: To compare the effects of two adjuvant formulations of purified and inactivated SIV delta, in the Rhesus Macaque, in terms of specific humoral and cellular immune responses, and protection. MATERIAL AND METHODS: The immunogen, delta strain of SIV, was produced on Hut 78 cells, banded onto consecutive sucrose gradients, and inactivated with beta-propiolactone and gamma-irradiation. One group of 5 animals (A) received 3 IM doses of 100 micrograms

immunogen in an oil-in-water emulsion using RIBI adjuvant containing mycobacterial cell wall skeleton and monophospholipid (CWS/MPL). A second group of 5 monkeys (B) received 3 IM doses of 100 micrograms immunogen in a water-in-oil emulsion using IFA containing CWS/MPL, followed by 1 IM dose of 100 micrograms immunogen in IFA. Animals were vaccinated on days 0, 56 and 194. Specific ELISA, Western Blot, and lymphocyte proliferative responses to SIV delta were performed every two weeks. Neutralizing antibodies titers, blood cell counts, CD4, CD8 cell counts, blood chemistry, and anti-cell antibodies were also monitored. Three months after the last dose animals were challenged IV with 10 to 100 AID50 of cell-free SIVmac251 produced on rhesus PBLs, along with a non vaccinated control group. RESULTS: In group A, anti SIV antibody titers transiently reached 4 to 5 log10 after 2-3 injections but no specific proliferative responses were detectable. Group B animals showed high (5-6 log10) and more stable titers after 1-2 injections; high proliferative responses were detected in this group. After the 3rd injection, proliferative responses were seen as early as 48 hours after initiating in vitro immunogen stimulation, with an optimum at 72 hours. Group B, but not Group A, animals exhibited neutralizing antibodies on the day of challenge. Monkeys in both groups developed anti-human-cell antibodies Autoimmune-like symptoms were observed in 2 animals in group B. The outcome of challenge is under investigation CONCLUSION: CWS/MPL(RIBI adjuvant) induced immunologic responses comparable to those produced by alum and by MDP-containing adjuvants when used with a similar immunogen, as previously reported by other investigators. The CWS/MPL+IFA adjuvant produced stronger immunological responses (both humoral and cell-mediated); however, autoimmune-like symptoms were observed in 2/5 animals. Studies with other adjuvants and combinations of adjuvants are underway for the purpose of identifying those that produce protective immunologic responses without inducing undesirable side effects.

CT Check Tags: Animal; Comparative Study
Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
*Adjuvants, Immunologic
*Cord Factors: IM, immunology
Freund's Adjuvant: IM, immunology
Immunity, Cellular
*Lipid A: AA, analogs & derivatives
Lipid A: IM, immunology
*Macaca mulatta: IM, immunology
Simian Acquired Immunodeficiency Syndrome: PC, prevention & control
*SIV: IM, immunology
Vaccines, Inactivated: IM, immunology
*Viral Vaccines
Viral Vaccines: IM, immunology

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 9007-81-2 (Freund's Adjuvant)

CN 0 (Adjuvants, Immunologic); 0 (Cord Factors); 0 (Lipid A); 0 (Ribi adjuvant); 0 (Vaccines, Inactivated); 0 (Viral Vaccines)

L76 ANSWER 21 OF 38 AIDSLINE
AN 1992:11199 AIDSLINE
DN ICA8-92400280
TI Protection of rhesus macaques from cell-free and cell-associated SIV challenge, by vaccination with SIV iscoms or MDP adjuvanted inactivated SIV.
AU De Vries P; Heeney J; Morein B; Osterhaus A D
CS Laboratory of Immunobiology, RIVM, Bilthoven, The Netherlands.

SO Int Conf AIDS, (1992). Vol. 8, No. 1, pp. We52 (Abstract No. WeD 1042).
CY Netherlands
DT Abstract
FS ICA8
LA English
EM 199212
AB OBJECTIVES: Comparison of protection afforded by iscome and MDP adjuvanted whole inactivated virus in a SIV-macaque model. METHODS: Eight macaques (Macaca mulatta) were vaccinated four times with an SIV iscom vaccine, eight with an MDP adjuvanted whole inactivated SIV vaccine, four with a measles virus (MV) iscom vaccine and four with an MDP adjuvanted inactivated whole MV vaccine. They were all challenged with either 10MID50 of the homologous cell-free SIVmac251 (32H) propagated in C8166 cells or with 10MID50 of SIV-infected PBMC directly taken from a monkey suffering from AIDS after infection with the SIVmac251 (32H) strain. RESULTS: All the monkeys vaccinated with SIV-MDP and SIV-iscom and challenged with cell-free SIVmac251 (32H) were protected from developing SIV viraemia, whereas all the MV-MDP and MV-iscom vaccinated monkeys developed SIV-viraemia within four weeks after cell-free challenge. Also all the MV-MDP and MV-iscom vaccinated animals challenged with SIV infected PBMC developed viraemia within 2 weeks. Two out of four SIV-MDP vaccinated and two out of four SIV-iscom vaccinated monkeys challenged with SIV infected PBMC were protected from SIV viraemia. The data were confirmed by serological tests and PCR analyses. CONCLUSION: This is the first demonstration that vaccination can protect macaques from challenge with SIV infected PBMC. This protection should be attributed to immunization with SIV-specific antigens since the challenge was carried out directly with SIV infected PBMC of the homologous species.
CT Check Tags: Animal; Comparative Study
Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage
Macaca mulatta
*Simian Acquired Immunodeficiency Syndrome: PC, prevention & control
*SIV: IM, immunology
Vaccines, Inactivated: AD, administration & dosage
*Viral Vaccines: AD, administration & dosage
Viremia: PC, prevention & control
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**
CN 0 (Vaccines, Inactivated); 0 (Viral Vaccines)

L76 ANSWER 22 OF 38 AIDSLINE
AN 1992:11016 AIDSLINE
DN ICA8-92400075
TI Phase 1 dose escalation MTP-PE study of an HIV-1 gp120 vaccine in sero-negative adults.
AU Kahn J; Chernoff D; Sinangil F; Murcar N; Wynne D; Coleman R; Haigwood N; Steimer K; Dekker C
CS AIDS Division, San Francisco General Hospital, University of California.
SO Int Conf AIDS, (1992). Vol. 8, No. 1, pp. Mo9 (Abstract No. MoB 0025).
CY Netherlands
DT Abstract
FS ICA8
LA English
EM 199212

AB OBJECTIVES: We conducted a phase 1 randomized double-blind study to determine safety and immunogenicity in HIV-seronegative adults of three injections of a vaccine composed of 25 micrograms of recombinant HIV gp 120 antigen combined with MF 59 emulsion containing a muramyl tripeptide covalently linked with dipalmitoyl phosphatidylethanolamine (MTP-PE) at different concentrations. Specifically we examined the ability of the candidate vaccine to elicit ELISA and neutralizing antibodies against HIV, the immunologic stimulatory properties of the adjuvant as well as the effects of the vaccine candidate. METHODS: The vaccine antigen is recombinant gp 120 from the SF2 strain of HIV-1, expressed in Chinese hamster ovary cells. The gp 120 vaccine is fully glycosylated and exhibits CD4 binding activity. Forty-two healthy HIV-seronegative adult men and women, with normal laboratory studies and without identifiable high-risk behavior for HIV infection were vaccinated. Vaccination occurred at day 0, 1 month and at 6 months. Vaccinees will be followed for 6 months after last injection. Subjects were entered into the study according to the following design: TABULAR DATA, SEE ABSTRACT VOLUME. Each vaccine contained MF59 emuslion and each subject in the different groups received MTP-PE dosing as scheduled above. Two subjects in each group were randomized to receive placebo-antigen while 6 received gp 120 at 25 micrograms dose. RESULTS: To date, subjects tolerated vaccination well. Symptoms reported include mild muscle aches, headache, low grade fevers. All symptoms were graded as mild. One subject in group 3 had a transient increase in liver function studies and bilirubin that resolved without interruption of the vaccine administration. One subject in Group 3 left the study. Five subjects in groups 1, 2 and 3, after only 2 immunizations, have developed HIV neutralizing antibodies. No subject has yet received a third immunization, and not all individuals in Groups 4 and 6 have received a second immunization. CONCLUSIONS: Initial information suggests that this candidate HIV vaccine is well tolerated. The relative toxicities of the candidate vaccine, the development of neutralizing antibodies and the immunologic effects of vaccination will be presented. Ultimate study conclusions will be based upon the complete and final data set.

CT Check Tags: Human
Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives
Adult
*AIDS Vaccines
Double-Blind Method
Enzyme-Linked Immunosorbent Assay
*HIV Antibodies: BI, biosynthesis
HIV Antibodies: IM, immunology
HIV Envelope Protein gp120: AD, administration & dosage
*HIV Envelope Protein gp120: IM, immunology
*HIV Seropositivity
*HIV-1: IM, immunology
Immunization, Secondary
Neutralization Tests
Phosphatidylethanolamines
Recombinant Proteins: AD, administration & dosage
Recombinant Proteins: IM, immunology
Safety
*Vaccination
*Vaccines, Synthetic

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 83461-56-7

(CGP 19835 A)
CN 0 (AIDS Vaccines); 0 (HIV Antibodies); 0 (HIV Envelope Protein gp120); 0 (Phosphatidylethanolamines); 0 (Recombinant Proteins); 0 (Vaccines, Synthetic)

L76 ANSWER 23 OF 38 AIDSLINE
AN 1992:11009 AIDSLINE
DN ICA8-92400068
TI Vaccine protection from SIV infected cell challenge is MHC class I related.
AU Heeney J; Bontrop R; Van Els C; De Vries P; Jonker M; Osterhaus A
CS Dept. of Chronic and Infectious Diseases, ITRI-TNO, Rijswijk, The Netherlands.
SO Int Conf AIDS, (1992). Vol. 8, No. 1, pp. Mo7 (Abstract No. MoA 0018).
CY Netherlands
DT Abstract
FS ICA8
LA English
EM 199212
AB OBJECTIVE: To determine if vaccine protection against infected cells is related to the MHC type of donor and recipient. METHODS: Twenty four MHC typed Macaca mulatta vaccinated with either formalin inactivated whole SIV adjuvanted with MDP (n = 8) or in ISCOM (n = 8) preparations. Controls included measle virus (MV) MDP (n = 4) or ISCOM (n = 4) controls. Half of the group was homologously challenged with 10 MID50 of cell-free SIVmac32H. The other half of the group was challenged with 10 MID50 of peripheral blood mononuclear (PBMCs) from an SIVmac32H infected macaque with AIDS. RESULTS: All SIV vaccinated animals challenged with homologous cell-free SIVmac32H were protected. Antibody responses against the cell line used to produce the vaccine did not correlate with protection (Osterhaus et al., Nature 1991; 355, 685). Of the animals challenged with an equivalent infectious dose of PBMCs from an SIV infected macaque only half were protected. Animals protected from the cell associated challenge shared a particular MHC class I allele with the donor of the infected cells. CONCLUSION: These results suggest that vaccine protection against cells infected with SIV (or HIV) may recognise antigen in the context of an MHC molecule which is shared between the donor and vaccinated recipient, facilitating a protective cell mediated immune response.
CT Check Tags: Animal; Comparative Study
Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
Adjuvants, Immunologic
*Histocompatibility Antigens Class I: PH, physiology
ISCOMs: IM, immunology
Leukocytes, Mononuclear: IM, immunology
Leukocytes, Mononuclear: MI, microbiology
Leukocytes, Mononuclear: TR, transplantation
*Macaca mulatta: IM, immunology
Measles Vaccine
*Simian Acquired Immunodeficiency Syndrome: PC, prevention & control
*SIV: IM, immunology
Vaccination
*Viral Vaccines: IM, immunology
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**
CN 0 (Adjuvants, Immunologic); 0 (Histocompatibility Antigens Class I); 0 (ISCOMs); 0 (Measles Vaccine); 0 (Viral Vaccines)

AB Rhesus macaques (Macaca mulatta) immunized with an inactivated whole SIVmac vaccine and muramyl dipeptide (MDP), incomplete Freund's adjuvant (IFA), or aqueous suspension were challenged intravenously with 0.1 TCID50 of cell-free SIVmac. Whereas virus was readily recovered from the peripheral blood lymphocytes of 10 of 10 nonvaccinated controls following this challenge dose, virus was not recovered from the three animals that received the vaccine with MDP nor from one of two animals that received the vaccine with IFA and one of three animals that received the aqueous vaccine. The animals that were protected against challenge were those that had detectable SIV antibody response to the envelop, both the outer glycoprotein (gp120) and the truncated transmembrane glycoprotein (gp31). Protected monkeys tended to have higher titers of syncytial inhibition antibody prior to challenge. An anamnestic response after challenge was observed only in the vaccinated monkeys that became infected. Vaccinated animals that became challenge-infected tended to live longer than infected controls. These results confirm those at two other primate centers and indicate that killed whole SIV vaccines can protect against low challenge doses of SIV and prevent early death in those monkeys that do become infected. The mechanism of this protection remains undetermined. This finding adds optimism to the possibility of an eventual AIDS vaccine.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
Antibodies, Viral: BI, biosynthesis
Antigens, Viral: IM, immunology
Base Sequence
Cell Line
Freund's Adjuvant: IM, immunology
Giant Cells: CY, cytology
Immunoblotting
Immunoenzyme Techniques
Immunologic Memory
Macaca mulatta
Molecular Sequence Data
*Simian Acquired Immunodeficiency Syndrome: PC, prevention & control
*SIV: IM, immunology
Vaccination
Vaccines, Inactivated: IM, immunology
Viral Envelope Proteins: IM, immunology
*Viral Vaccines: IM, immunology

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 9007-81-2 (Freund's Adjuvant)

CN 0 (Antibodies, Viral); 0 (Antigens, Viral); 0 (Vaccines, Inactivated); 0 (Viral Envelope Proteins); 0 (Viral Vaccines)

L76 ANSWER 28 OF 38 AIDSLINE
AN 1991:4760 AIDSLINE
DN ASM90-905018
TI Protection for macaques against SIVmac challenge using an inactivated whole virus vaccine.
AU Carlson J R; McGraw T P; Keddie E; Jennings M B; Vowels B; Gardner M B
CS Med. Pathology, Univ. California, Davis.
SO Abstr Annu Meet Am Soc Microbiol, (1990). Vol. 90, pp. 338 (Abstract No. T-13).
ISSN: 0094-8519.
CY United States

DT Abstract
FS ASM90
LA English
EM 199107
AB Rhesus monkeys were immunized by multiple inoculations with purified, inactivated SIVmac (ISIV). Experimental groups included animals that received the SIVmac immunogen in muramyl dipeptide, incomplete Freund's adjuvant, or in aqueous suspension. ISIV immunized animals developed anti-SIV antibodies and positive, SIV specific, T cell proliferation responsiveness. Monkeys were challenged with infectious cell-free SIVmac by an intramuscular inoculation. SIV isolation from peripheral blood was used to evaluate infection following the challenge. None of the 3 animals that received ISIV/MDP became viremic after challenge. On of 2 animals that received ISIV/IFA, 2/3 that received Aq ISIV and 4/4 controls became viremic. These results confirm two recent reports that vaccination with inactivated whole virus can protect macaques against challenge with live SIV.
CT Check Tags: Animal
Acetylmuramyl-Alanyl-Isoglutamine
Antibodies, Viral: IM, immunology
Freund's Adjuvant
Lymphocyte Transformation
Macaca mulatta
*Simian Acquired Immunodeficiency Syndrome: PC, prevention & control
*SIV: IM, immunology
SIV: IP, isolation & purification
T-Lymphocytes: IM, immunology
Vaccines, Inactivated
*Viral Vaccines
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 9007-81-2 (Freund's Adjuvant)
CN 0 (Antibodies, Viral); 0 (Vaccines, Inactivated); 0 (Viral Vaccines)

L76 ANSWER 29 OF 38 AIDSLINE
AN 1991:4709 AIDSLINE
DN PRIM8-900036
TI Protection of rhesus macaques from infection with SIVMAC using a formalin inactivated whole virus preparation.
AU Cranage M P; Cook N; Thompson A; Greenaway P J; Baskerville A
CS Public Health Laboratory Service Centre for Applied Microbiology and Research, Porton Down, Salisbury SP4 OJG, United Kingdom.
SO Symp Nonhum Primate Models AIDS, (1990). Vol. 8, pp. 52 (Abstract No. 36).
CY United States
DT Abstract
FS PRIM8
LA English
EM 199107
AB Eight rhesus macaques were inoculated with formalin inactivated SIVMAC251 (32H isolate) prepared from cell free supernatant of infected C8166 cells by gel filtration chromatography. Each animal received a total of four intramuscular inoculations of 500 mug administered in threonyl muramyl dipeptide adjuvant (kindly provided by Syntex Corporation). Four animals received a primary inoculation, two boosts at monthly intervals and a final boost two months later and were then challenged intravenously, together with two control animals, two weeks later with 10 MID50 of homologous virus. Virus was isolated from control animals at 12, 27, 40 and 55 days (to

date) post challenge, whereas no virus was recovered from the vaccinated group. These results were confirmed by PCR analysis of DNA from monkey PBL's (personal communication - P. Kitchin, NIBSC). A further four animals were given a primary vaccination, two monthly boosts and a final boost four months later and were then challenged two weeks later with 10 MID50 of SIVDELTAB670 (kindly provided by Dr Murphey Corb). Data from the heterologous challenge group are not yet available at the time of writing. All vaccinated animals made strong humoral immune responses. Preliminary data on the analysis of the protective immune response will be presented.

CT Check Tags: Animal
Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
Antibodies, Viral: BI, biosynthesis
Cells, Cultured
Chromatography, Gel
DNA, Viral: AN, analysis
*Formaldehyde: PD, pharmacology
Leukocytes, Mononuclear: MI, microbiology
Macaca mulatta
Polymerase Chain Reaction
*Simian Acquired Immunodeficiency Syndrome: PC, prevention & control
SIV: DE, drug effects
SIV: GE, genetics
*SIV: IM, immunology
Vaccination
Vaccines, Inactivated
*Viral Vaccines

RN 50-00-0 (Formaldehyde); **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**

CN 0 (Antibodies, Viral); 0 (DNA, Viral); 0 (Vaccines, Inactivated); 0 (Viral Vaccines)

L76 ANSWER 30 OF 38 AIDSLINE
AN 1991:4706 AIDSLINE
DN PRIM8-900033
TI SIV vaccine protection of rhesus macaques.
AU Carlson J R; McGraw T P; Keddie E; Yee J L; Rosenthal A; Langlois A J; Dickover R; Donovan R; Luciw P A; Jennings M B; et al
CS Departments of Pathology and Internal Medicine, School of Medicine, California Primate Research Center, University of California, Davis.
SO Symp Nonhum Primate Models AIDS, (1990). Vol. 8, pp. 49 (Abstract No. 33).
CY United States
DT Abstract
FS PRIM8
LA English
EM 199107
AB Rhesus macaques (M.mulatta) immunized with an inactivated whole SIVmac vaccine and muramyl dipeptide (MDP) incomplete Freund's adjuvant (IFA) or aqueous suspension were challenged intravenously with 10 animal infectious doses (ID) (0.1 TCID/50) of cell free SIVmac. Whereas virus was readily recovered from the PBLs of 10 of 10 non-vaccinated controls following this challenge dose, virus was not recovered from the three animals that received the vaccine with MDP nor from one of two animals that received the vaccine with IFA and one of three animals that received the aqueous vaccine. The animals that were protected against challenge were those that had more detectable SIV antibody response to the envelope, both the outer glycoprotein (gp120) and the truncated transmembrane

FS MED; Priority Journals
LA English
OS MEDLINE 91069612
EM 199103
AB Cultured monocyte-derived macrophages were productively infected with human immunodeficiency virus in vitro. Treatment of these cells shortly after infection and several times thereafter with the free form of MTP-PE had an inhibitory effect on virus production. When the liposomal formulation of MTP-PE was used, higher levels of protection were achieved. The drug was not only effective when added to cells immediately after infection, but it also reduced virus production by cells with an established infection. When the liposomal formulation of MTP-PE was used only one treatment was required to achieve maximal effects. During these studies it was noted that the placebo liposomes had some effect in reducing the reverse transcriptase levels found in the supernatants of infected cells. This reduction could not be explained by direct cytotoxic effect. Both free and liposomal MTP-PE lipid significantly prevented formation of giant cells during the course of infection as well as reduced the cell associated viral antigen.
CT Check Tags: Human; In Vitro
***Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives**
Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage
Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology
Antiviral Agents
Dose-Response Relationship, Drug
Drug Carriers
*HIV: DE, drug effects
HIV: EN, enzymology
HIV: PH, physiology
Liposomes
Macrophages: DE, drug effects
Macrophages: EN, enzymology
Macrophages: MI, microbiology
Phosphatidylethanolamines: AD, administration & dosage
*Phosphatidylethanolamines: PD, pharmacology
RNA-Directed DNA Polymerase: AI, antagonists & inhibitors
*Virus Replication: DE, drug effects
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 83461-56-7 (CGP 19835 A)
CN EC 2.7.7.49 (RNA-Directed DNA Polymerase); 0 (Antiviral Agents); 0 (Drug Carriers); 0 (Liposomes); 0 (Phosphatidylethanolamines)

L76 ANSWER 33 OF 38 AIDSLINE
AN 1990:16015 AIDSLINE
DN ICA6-40105090
TI Novel muramyl tripeptide (MTP-PE) adjuvant formulations for enhancement of immunity to recombinant HIV-1 gp120 envelope antigens.
AU Van Nest G; Barchfeld G; Haigwood N; Ott G; Wentworth P; Steimer K
CS Chiron Corporation, Emeryville, California, USA.
SO Int Conf AIDS, (1990). Vol. 6, No. 2, pp. 326 (Abstract No. 1050).
CY United States
DT Abstract
FS ICA6
LA English
EM 199012

*Monocytes: MI, microbiology
Tumor Necrosis Factor: BI, biosynthesis
Virus Replication: DE, drug effects
Zidovudine: PD, pharmacology
RN 30516-87-1 (Zidovudine); 4097-22-7 (Dideoxyadenosine); **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 82115-62-6 (Interferon Type II)
CN 0 (monophosphoryl lipid A); 0 (Cord Factors); 0 (Glycolipids); 0 (Interleukin-1); 0 (Lipid A); 0 (Tumor Necrosis Factor)

L76 ANSWER 36 OF 38 AIDSLINE
AN 1990:1882 AIDSLINE
DN MED-90069604
TI A formalin-inactivated whole SIV vaccine confers protection in macaques.
AU Murphey-Corb M; Martin L N; Davison-Fairburn B; Montelaro R C; Miller M; West M; Ohkawa S; Baskin G B; Zhang J Y; Putney S D; et al
CS Delta Regional Primate Research Center, Tulane University, Covington, LA 70434.
SO SCIENCE, (1989). Vol. 246, No. 4935, pp. 1293-7. Journal code: UJ7. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals; Cancer Journals
LA English
OS MEDLINE 90069604
EM 199003
AB A vaccine against human immunodeficiency virus (HIV) would be highly effective in stopping the acquired immunodeficiency syndrome (AIDS) epidemic. A comprehensive evaluation of potential vaccine methodologies can be made by means of the simian model for AIDS, which takes advantage of the similarities in viral composition and disease potential between simian immunodeficiency virus (SIV) infection of rhesus macaques and HIV infection in humans. Immunization with a formalin-inactivated whole SIV vaccine potentiated with either alum and the Syntex adjuvant threonyl muramyl dipeptide (MDP) or MDP alone resulted in the protection of eight of nine rhesus monkeys challenged with ten animal-infectious doses of pathogenic virus. These results demonstrate that a whole virus vaccine is highly effective in inducing immune responses that can protect against lentivirus infection and AIDS-like disease.
CT Check Tags: Animal
Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
Adjuvants, Immunologic: AD, administration & dosage
Alum Compounds: AD, administration & dosage
Antibodies, Viral: BI, biosynthesis
Chromatography, High Pressure Liquid
Disease Models, Animal
Formaldehyde
Immunization, Secondary
Leukocyte Count
Lymphocytes: IM, immunology
Lymphocytes: MI, microbiology
Macaca mulatta
*Retroviridae Infections: PC, prevention & control
Retroviridae Proteins: IM, immunology
*SIV: IM, immunology
SIV: IP, isolation & purification
Vaccines, Inactivated: AD, administration & dosage

Vaccines, Inactivated: IM, immunology
Viral Vaccines: AD, administration & dosage
*Viral Vaccines: IM, immunology
Virion: IM, immunology

RN 10043-01-3 (aluminum sulfate); 50-00-0 (Formaldehyde); **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 66112-59-2 (N-acetylmuramyl-threonyl-isoglutamine)

CN 0 (Adjuvants, Immunologic); 0 (Alum Compounds); 0 (Antibodies, Viral); 0 (Retroviridae Proteins); 0 (Vaccines, Inactivated); 0 (Viral Vaccines)

L76 ANSWER 37 OF 38 AIDSLINE
AN 1988:5858 AIDSLINE
DN ICDB-88647963
TI DEVELOPMENT OF AN ADJUVANT FORMULATION THAT CAN ELICIT PROTECTIVE IMMUNITY AGAINST RETROVIRUSES.
AU Allison A C; Byars N E
CS Inst. of Biological Sciences, Syntex Res., Palo Alto, CA 94304.
SO (1987). Vaccines 87. Modern Approaches to New Vaccines: Prevention of AIDS and Other Viral, Bacterial, and Parasitic Diseases. Chanock RM et al, eds. New York, Cold Spring Harbor Laboratory, p. 56-9, 1987.
DT (MEETING PAPER)
FS ICDB
LA English
OS CANCERLIT 88647963
EM 198812
AB Traditional virus vaccines have included attenuated live viruses, which elicit both humoral and cell-mediated immunity (CMI), and inactivated viruses or their components, which elicit circulating IgG antibodies in sufficient concentration to protect humans from disease. The cloning and expression of the genes for the hepatitis-B virus surface (HBsAg) and core (HBcAg) antigens in yeast and Escherichia coli, and the licensing by the Food and Drug Administration of the former in a vaccine, open up a new chapter in the history of immunization. The full promise of this approach requires the development of an adjuvant formulation that, with virus and other subunit antigens, elicits the production of antibodies of protective isotypes, CMI, and memory in both T- and B-lymphocyte populations. The development of an adjuvant formulation is reported that meets these requirements and appears to be free from unacceptable side effects. A nontoxic small molecule that would be the equivalent of the mycobacterial cell-wall component of Freund's complete adjuvant was identified: the threonyl analog of muramyl dipeptide (MDP). A nonionic detergent with unusual properties--Pluronic L121 triblock polymer--was formulated. Both the MDP analog and Pluronic formulation are required for optimal adjuvant activity: the combination is termed Syntex Adjuvant Formulation-1 or SAF-1. This formulation does not produce tissue damage or elicit an inflammatory reaction at injection sites, and no systemic reaction is demonstrable. A variety of viral subunits, monoclonal immunoglobulins, and other antigens have, when administered im or sc in SAF-1, elicited high titers of antibodies and CMI. Examples of the use of SAF-1 to elicit immunity to viruses include the development of an efficacious vaccine against feline leukemia virus, protection of rhesus monkeys against simian acquired immune deficiency syndrome virus (unsuccessful), and evoking high titers of antibodies using HBsAg in laboratory animals. Collaborative studies have also shown primary and secondary

responses to recombinant HBsAg and HBcAg in SAF-1, comparable to those in Freund's complete adjuvant. (6 Refs)
CT Check Tags: Animal
Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives
Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
Acquired Immunodeficiency Syndrome: IM, immunology
Acquired Immunodeficiency Syndrome: PC, prevention & control
*Adjuvants, Immunologic
Antibody Formation
Cats
HIV: IM, immunology
Leukemia Virus, Feline: IM, immunology
Macaca mulatta
*Retroviridae: IM, immunology
Vaccination
Viral Vaccines: AD, administration & dosage
*Viral Vaccines: IM, immunology
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**
CN 0 (Adjuvants, Immunologic); 0 (Viral Vaccines)

L76 ANSWER 38 OF 38 AIDSLINE
AN 1988:5705 AIDSLINE
DN MED-88288096
TI Possible treatment of AIDS patients with live lactobacteria.
AU Tihole F
SO MEDICAL HYPOTHESES, (1988). Vol. 26, No. 1, pp. 85-8.
Journal code: M0M. ISSN: 0306-9877.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 88288096
EM 198811
AB The enhancement of antimicrobial resistance and immunomodulatory action, and the anabolic effect caused by the consumption of live lactobacteria as a dietary adjunct are proposed by the author as sufficient reasons to test lactobacterial preparations in patients with AIDS. The problem of dosage is discussed and a practical solution presented.
CT Check Tags: Human
Acetylmuramyl-Alanyl-Isoglutamine: TU, therapeutic use
Acquired Immunodeficiency Syndrome: IM, immunology
*Acquired Immunodeficiency Syndrome: TH, therapy
Immunity, Natural
*Immunization: MT, methods
*Lactobacillus acidophilus
*Opportunistic Infections: TH, therapy
Phagocyte Bactericidal Dysfunction: TH, therapy
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**

```
=> d his


     (FILE 'HOME' ENTERED AT 09:31:58 ON 08 DEC 1998)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 09:32:03 ON 08 DEC 1998
L1             2 S 74817-61-1 OR 60355-78-4

     FILE 'BIOSIS' ENTERED AT 09:32:36 ON 08 DEC 1998
L2            74 S L1 OR MURABUTIDE OR MURAMETIDE
                E RETROVIR/BC
L3             0 S E5 AND L2
L4             2 S E4-E8 AND L2

=> fil biosis

FILE 'BIOSIS' ENTERED AT 09:33:42 ON 08 DEC 1998
COPYRIGHT (C) 1998 BIOSIS(R)

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 18 November 1998 (981118/ED)
CAS REGISTRY NUMBERS (R) LAST ADDED: 18 November 1998 (981118/UP)


=> d all l4


L4   ANSWER 1 OF 2  BIOSIS  COPYRIGHT 1998 BIOSIS
AN  97:420005  BIOSIS
DN  99719208
TI  Construction of peptide immunogens and novel delivery systems
    (liposomes and ISCOMS) against HIV and gag sequences with
  murabutide as an immunoadjuvant.
AU  Agrawal L; Sabhnani L; Rao D N
CS  AIIMS, New Delhi-110029, India
SO  17th International Congress of Biochemistry and Molecular Biology in
    conjunction with the Annual Meeting of the American Society for
    Biochemistry and Molecular Biology, San Francisco, California, USA,
    August 24-29, 1997. FASEB Journal 11 (9). 1997.  A983. ISSN:
    0892-6638
DT  Conference
LA  English
PR  Biological Abstracts/RRM Vol. 049 Iss. 010 Ref. 171318
ST  MEETING ABSTRACT; HUMAN IMMUNODEFICIENCY VIRUS TYPE 1; HIV-1;
    LIPOSOMAL DRUG DELIVERY SYSTEM; ISCOMS; T CELL; PND V3;
    IMMUNOSTIMULANT-DRUG; CONSTRUCTION; PEPTIDE IMMUNOGEN; HUMAN
    IMMUNODEFICIENCY VIRUS VACCINE; PHARMACOLOGY; METHODOLOGY;
    BIOCHEMISTRY AND BIOPHYSICS; DRUG DELIVERY METHOD; BLOOD AND
    LYMPHATICS; IMMUNE SYSTEM
RN  74817-61-1 (MURABUTIDE)
CC  General Biology-Symposia, Transactions and Proceedings of
    Conferences, Congresses, Review Annuals  00520
    Cytology and Cytochemistry-Animal  *02506
    Biochemical Studies-Proteins, Peptides and Amino Acids  *10064
    Biophysics-Molecular Properties and Macromolecules  *10506
```

Biochemical Studies-Carbohydrates 10068
Pathology, General and Miscellaneous-Inflammation and Inflammatory Disease *12508
Pathology, General and Miscellaneous-Therapy *12512
Cardiovascular System-Heart Pathology *14506
Blood, Blood-Forming Organs and Body Fluids-Lymphatic Tissue and Reticuloendothelial System *15008
Endocrine System-General *17002
Muscle-Pathology *17506
Nervous System-Pathology *20506
Pharmacology-Endocrine System *22016
Pharmacology-Immunological Processes and Allergy *22018
Toxicology-Pharmacological Toxicology *22504
Medical and Clinical Microbiology-Virology *36006
Chemotherapy-Antiviral Agents *38506

BC Picornaviridae 02619
Retroviridae 02623
Muridae 86375

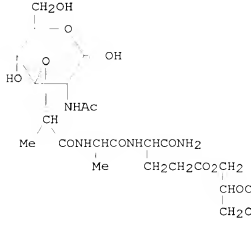
.gtoreq.1 natural or recombinant and preferably human **cytokine** with .gtoreq.1 muramyl peptide selected from those which, when administered in vivo together with an **interferon**, also induce an increased in vivo prodn. of an interleukin-1 receptor antagonist, but preferably do not induce any increase in TNF, IL-8 and IL-1 **cytokines**. The compn. is useful for antiviral and antitumor therapies and/or for promoting restoration of the hematopoietic system, particularly in individuals with a weakened immune system. Studies of the effect of e.g. a mutabutide-**interferon** combination in an animal toxic shock model are described.

IT **60355-78-4, Murametide 60355-78-4D, Murametide**, homologs **60355-79-5 60355-79-5D**, homologs **74817-61-1, Murabutide 74817-61-1D, Murabutide**, homologs **83869-56-1, GM-CSF 127088-99-7 127179-83-3**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Therapeutic combination of muramyl peptide and **cytokine**)

L62 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1994:407303 HCAPLUS
DN 121:7303
TI Muramyl dipeptide derivative in adjuvant not inducing response to autoantigenic determinants
IN Chedid, Louis; Audibert, Francoise; Lefrancier, Pierre
PA **Vacsyn France SA, Fr.**
SO Fr. Demande, 14 pp.
CODEN: FRXXBL
DT **Patent**
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2692148	A1	19931217	FR 92-7126	19920612
	FR 2692148	B3	19940819		

GI



I

AB An adjuvant is disclosed for humoral or cellular immune response or both but without induction of an autoimmune condition from a response to autoantigenic determinants. The adjuvant contains N-acetylmuramyl-D-alanyl-D-[.gamma.-(sn-dipalmitoyl)glycerol]isoglutamine (I). The adjuvant is useful for vaccine compns. which may contain autoantigens, eg. an **AIDS** virus vaccine using virus derived from cultures of human cells or cell lines derived therefrom.

IT **127088-99-7**
RL: BIOL (Biological study)
(adjuvant contg., for lack of response to autoantigen)

L62 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1994:215331 HCAPLUS
DN 120:215331
TI Humoral and cell-mediated immunity adjuvant composition inducing no response to autoantigenic determinants
IN Chedid, Louis; Audibert, Francoise; Lefrancier, Pierre
PA **Vacsyn S.A.**, **Fr.**
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT **Patent**
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9325236	A1	19931223	WO 93-FR569	19930614
	W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	FR 2692149	A1	19931217	FR 92-7125	19920612
	FR 2692149	B1	19950609		
	AU 9343318	A1	19940104	AU 93-43318	19930614
PRAI	FR 92-7125	19920612			
	WO 93-FR569	19930614			

OS MARPAT 120:215331
GI

AU 9748320 A1 19980312 AU 97-48320 19971211
PRAI US 93-48976 19930416
US 90-589422 19900927
US 93-8092 19930122
WO 94-SE340 19940415
AB Novel peptides are disclose which correspond to epitopes of the **HIV**-1 gp120env protein. These antigenic peptides induce antibody-dependent cellular cytotoxicity (ADCC) against **HIV**, and thus are useful in immunization against **HIV** infection and induction of a heightened immune response to **HIV**. Among 41 synthetic peptides covering the entire sequence of **HIV** gp120, 14 showed an ADCC index value greater than 0.5 at a dilu. greater than 1:30, in an amt. effective to induce an immune response in a mammal together with a pharmaceutically acceptable carrier. The vaccine compn. further comprises an adjuvant such as Freund's complete adjuvant, Freund's incomplete adjuvant, muramyl dipeptide, levamisole, isoprinosine, or tuftsin.
IT **53678-77-6**, Muramyl dipeptide
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adjuvant; peptides for use in vaccination and induction of neutralizing antibodies against **human immunodeficiency** virus)

L62 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1995:240035 HCAPLUS
DN 122:23868
TI Therapeutic compositions for use in humans, characterized by a combination of a muramyl peptide and a **cytokine**
IN Chedid, Louis; **Bahr, Georges**; Lefrancier, Pierre
PA **Vacsyn S. A., Fr.**
SO PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9421275	A1	19940929	WO 94-FR307	19940321
	W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	FR 2702659	A1	19940923	FR 93-3230	19930319
	FR 2702659	B1	19950825		
	FR 2703251	A1	19941007	FR 93-3787	19930331
	FR 2703251	B3	19950804		
	AU 9462856	A1	19941011	AU 94-62856	19940321
	EP 689449	A1	19960103	EP 94-910445	19940321
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 08511235	T2	19961126	JP 94-520726	19940321
PRAI	FR 93-3230	19930319			
	FR 93-3787	19930331			
	WO 94-FR307	19940321			

OS MARPAT 122:23868
AB A therapeutic compn. for use in humans comprises a combination of

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9502416	A1	19950126	WO 94-US7749	19940711
	W: AU, BR, CA, CN, JP, KR, NZ				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5562909	A	19961008	US 93-90841	19930712
	US 5529777	A	19960625	US 93-147781	19931104
	AU 9473286	A1	19950213	AU 94-73286	19940711
	AU 690567	B2	19980430		
	BR 9407397	A	19961105	BR 94-7397	19940711
	JP 09500132	T2	19970107	JP 94-504650	19940711
	EP 792161	A1	19970903	EP 94-923417	19940711
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
PRAI	US 93-90841	19930712			
	US 93-147781	19931104			
	WO 94-US7749	19940711			

AB Water-sol. polymers or polymeric hydrogels are used to encapsulate antigen to form vaccines. The antigen is mixed with a polymer soln. to form microparticles, and optionally, the polymer may be crosslinked to form stable microparticles. Preferred polymers are alginate and polyphosphazenes, and mixts. thereof. Microparticles can be administered parenterally or mucosally. Intranasal administration of antigens in a polyphosphazene or alginate microspheres induced a serum IgG response.

IT **53678-77-6**, Muramyldipeptide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrogel-microencapsulated vaccines)

L62 ANSWER 13 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1995:315804 HCAPLUS
DN 122:89368
TI Peptides for use in vaccination and induction of neutralizing antibodies against **human immunodeficiency** virus
IN Vahlne, Anders; Svennerholm, Bo; Rymo, Lars; Jeansson, Stig; Horal, Peter
PA Syntello Vaccine Development AB, Swed.
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT **Patent**
LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9423746	A1	19941027	WO 94-SE340	19940415
	W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2160696	AA	19941027	CA 94-2160696	19940415
	AU 9465153	A1	19941108	AU 94-65153	19940415
	EP 693938	A1	19960131	EP 94-912727	19940415
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09500096	T2	19970107	JP 94-523055	19940415
	US 5840313	A	19981124	US 95-493235	19950620

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

	FR 2724845	A1	19960329	FR 94-11460	19940926
	FR 2724845	B1	19970117		
	CA 2200993	AA	19960404	CA 95-2200993	19950926
	AU 9535699	A1	19960419	AU 95-35699	19950926
	EP 783319	A1	19970716	EP 95-932794	19950926
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 10506120	T2	19980616	JP 95-511445	19950926
PRAI	FR 94-11460	19940926			
	WO 95-FR1239	19950926			

OS MARPAT 125:26240

AB The use of non-toxic muramyl peptides, particularly **Murabutide** and **Murametide**, to prep. drugs for inhibiting **HIV** replication in humans, is disclosed. The muramyl peptides are capable of up to 100% inhibition of retroviral replication in primary host monocyte cultures.

IT **9001-92-7, Protease**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; muramyl peptide compns. with other agents for inhibiting **HIV** replication)

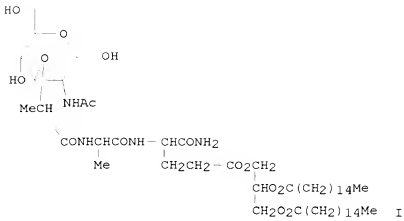
IT **60355-78-4, Murametide 74817-61-1, Murabutide**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (muramyl peptide compns. for inhibiting **HIV** replication)

IT **83869-56-1, GM-CSF**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (muramyl peptide compns. with other agents for inhibiting **HIV** replication)

L62 ANSWER 11 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1995:899025 HCAPLUS
DN 123:276025
TI Use of diesters of muramyl peptides in oral form as immunostimulating agents
IN Chedid, Louis; Audibert, Francoise; Lefrancier, Pierre
PA **Vacsyn, S.A.**, **Fr.**
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT **Patent**
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9519777	A2	19950727	WO 95-FR77	19950124
	WO 9519777	A3	19960307		

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT,



AB A process is disclosed for the prepn. of a pharmaceutical compn. having a selective immune adjuvant action for humoral response or cell-mediated response, preferably both at once, directed against given antigens, in the absence of any induction of autoimmune disorder linked to a response to autoantigenic determinants. The adjuvant of the invention contains a muramyl peptide deriv. (Markush included), esp. MDP-DD-GDP (I). Absence of induction of autoimmune disorder (allergic encephalomyelitis) in guinea pigs following administration of a water-in oil emulsion of myelin basic protein (autoantigen) with I is described.

IT **127088-99-7**
RL: BIOL (Biological study)
(for adjuvant compn. with no response to autoantigenic determinants)

L62 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1993:122811 HCAPLUS
DN 118:122811
TI The control of the antibody isotype response to recombinant **human immunodeficiency** virus gp120 antigen by adjuvants
AU Bomford, R.; Stapleton, M.; Winsor, S.; McKnight, A.; Andronova, T.
CS Wellcome Res. Lab., Beckenham/Kent, BR3 3BS, UK
SO AIDS Res. Hum. Retroviruses (1992), 8(10), 1765-71
CODEN: ARHRE7; ISSN: 0889-2229
DT Journal
LA English
AB Both saponin and muramyl dipeptide (MDP) formulated with a squalane-in-water emulsion of large particle size prepd. with a vortex mixer were superior to Al(OH)3 as adjuvants for **HIV** gp120 in mice. All the adjuvants induced IgG1 antibody, but saponin elicited the highest titers of IgG2a. The secretion of interleukin-5 (IL-5) and **interferon**-.gamma. (IFN.gamma.) by lymph node cells cultured in vitro with gp120 was studied. All the cultures secreted IL-5, but only those from saponin-immunized mice produced IFN.gamma., suggesting that saponin is capable of activating both the Th1 and Th2 T-cell subsets. The titers of neutralizing antibodies were low with both MDP and saponin, and they occurred in mice which were also pos. for antibodies against a V3 loop peptide. Glucosaminylmuramyl dipeptide (GMDP) which is less

pyrogenic than MDP and a nonpyrogenic analog GMDPA, displayed equiv. adjuvant activity to MDP. The level and isotype compn. of antibodies induced by GMDP in combination with squalane emulsions depended on the dimension of the emulsion particles. With a large (2500 nm) particle size the response was confined to IgG1 in Balb/c mice, but when this was reduced to 150 nm by sonication the antibody response was increased and relatively high levels of IgG2a appeared in some mice.

IT **53678-77-6**, MDP
RL: BIOL (Biological study)
(squalane-in-water emulsion of, antibody isotype response to **human immunodeficiency** virus envelope glycoprotein regulation by)

L62 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1992:52347 HCAPLUS
DN 116:52347
TI Synthetic peptide thymosin .alpha.1-N-acetylmuramyl-L-Alanyl-D-isoGlutaminyl-L-Lysine
IN Prinzhaus, Gerhard
PA Germany
SO Ger. Offen., 2 pp.
CODEN: GWXXBX
DT **Patent**
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4010645	A1	19910814	DE 90-4010645	19900327

PRAI DE 90-4003354 19900210
AB The title peptide, and also the peptide minus the terminal lysine, stimulates immunoreactivity to thymosin .alpha.1 or thymosin .alpha.1 homologous regions of other proteins. It can be used in treatment of autoimmune disease and **AIDS** (no data).
IT **53678-77-6D**, peptide conjugates
RL: BIOL (Biological study)
(as immunogen for antibodies to thymosin .alpha.1)

L62 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1990:434478 HCAPLUS
DN 113:34478
TI Muramyl dipeptide inhibits replication of **human immunodeficiency** virus in vitro
AU Masihi, K. Noel; Lange, Werner; Rohde-Schulz, Beate; Chedid, Louis
CS Robert Koch Inst., West Berlin, Fed. Rep. Ger.
SO AIDS Res. Hum. Retroviruses (1990), 6(3), 393-9
CODEN: ARHRE7; ISSN: 0889-2229
DT Journal
LA English
AB In the search for compds. capable of inducing endogenous prodn. of **colony-stimulating** factor (CSF) and possessing activity against **human immunodeficiency** virus (**HIV**), an immunomodulator, muramyl dipeptide (MDP), was investigated. MDP exhibited an inhibitory activity against **HIV** infection of CD4+ H9 lymphocytes and U937 monocytoid cells. An inhibitor of viral reverse transcriptase, 2', 3'-dideoxyzadenosine, produced potent inhibition in cultures which were similarly infected with **HIV**. MDP could partially reduce prodn. in persistently **HIV**-infected KE37/1

```
        RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE
     US 4705756        A    19871110       US 85-734799      19850516
     AU 8659594        A1   19861204       AU 86-59594       19860516
     EP 222891         A1   19870527       EP 86-903840      19860516
        R:  AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE
     JP 63500264       T2   19880128       JP 86-503182      19860516
     US 4814247        A    19890321       US 87-34101       19870316
     US 4900679        A    19900213       US 88-236039      19880823
PRAI US 85-734799      19850516
     US 83-440540      19830126
     US 83-538783      19831004
     US 85-703120      19850219
     WO 86-US1075      19860516
     US 87-34101       19870316
AB   The effect of an immunomodulator on reaction parameters (e.g.
     clotting parameters) in a cellular hematol. fluid is an index of the
     presence of a pathol. condition (e.g. sepsis, premyocardial
     infarction, cancer, diabetes, AIDS). In cancer patients,
     the blood recalcification time (RT) in the presence of an
     immunomodulator (Escherichia coli endotoxin) (RTi) was lower than in
     normal volunteers, whereas RT in the absence of immunomodulator
     (RTv) was the same in the two groups. The thrombotic index
     (RTv/RTi) and percent difference of clotting [(RTv-RTi)/RTv .times.
     100] were higher in cancer patients than in normal subjects.
IT   53678-77-6
     RL: BIOL (Biological study)
        (blood coagulation parameters response to, diagnosis in relation
        to)

=> d his 164-


     (FILE 'REGISTRY' ENTERED AT 09:06:53 ON 08 DEC 1998)

     FILE 'HCAPLUS' ENTERED AT 09:07:57 ON 08 DEC 1998
L64            7 S L41 NOT L62

=> d bib abs hitrn tot


L64  ANSWER 1 OF 7  HCAPLUS  COPYRIGHT 1998 ACS
AN   1997:645517  HCAPLUS
DN   127:314522
TI   Study of the adjuvant activity of new MDP derivatives and purified
     saponins and their influence on HIV-1 replication in vitro
AU   Krivorutchenko, Yuri L.; Andronovskaja, Irina B.; Hinkula, Jorma;
     Krivoshein, Yuri S.; Ljungdahl-Stahle, Ewa; Pertel, Sergey S.;
     Grishkovets, Vladimir I.; Zemlyakov, Alexander E.; Wahren, Britta
CS   Department of Microbiology and Virology, Crimean Medical Institute,
     Simferopol, 333670, Ukraine
SO   Vaccine (1997), 15(12/13), 1479-1486
     CODEN: VACCDE; ISSN: 0264-410X
PB   Elsevier
DT   Journal
LA   English
AB   Muramyl dipeptide (MDP), eight new lipophilic MDP derivs. (MDPs) and
     three purified saponins were evaluated for their ability to induce
     immune responses in mice immunized with HIV-1 envelope
     protein rgp160 and for their ability to influence the HIV
```

-1 replication in vitro. Three of nine new synthetic MDP derivs. (.beta.-butyl-MDP, MTPO-26 and .beta.-cholesteryl-MDP) and one saponin (Taurosid I) have been shown to induce strong humoral immune responses to **HIV**-1 envelope glycoproteins rgp160 and rgp120. Three substances (.beta.-butyl-MDP, MDP-cholyl and .beta.-G27-MDP) induced high levels of T-cell stimulation to **HIV**-1 rgp160. .beta.-Butyl-MDP induced the strongest B- and T-cell responses to **HIV**-1 glycoproteins. Two substances (.beta.-butyl-MDP and Taurosid I) did not induce an enhancement of **HIV**-1 replication in vitro and can be considered as promising adjuvants.

IT **53678-77-6**, Muramyl dipeptide
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adjuvant activity of muramyl dipeptide derivs. and purified saponins and their influence on **HIV**-1 replication in vitro)

L64 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 1998 ACS
AN 1997:295348 HCAPLUS
DN 126:338421
TI Effects of saponins derived from Hedera taurica Carr and modified muramylpeptides on the in vitro reproduction of **human immunodeficiency** virus
AU Krivorutchenko, Yu. L.; Andronovskaya, I. B.; Chirva, V. Ya.; Pertel, S. S.; Grishkovets, V. I.; Zemlyakov, A. Ye.; Kuryanov, V. O.; Krivoshein, Yu. S.
CS Russia
SO Vopr. Virusol. (1997), 42(1), 34-36
CODEN: VVIRAT; ISSN: 0507-4088
PB Meditsina
DT Journal
LA Russian
AB The effects of muramyldipeptide (MDP), several MDP derivs., and saponins derived from Hedera taurica Carr. on the in vitro replication of **HIV**-1 in lymphoblasts were studied. The coeff. of alteration of the rate of **HIV** replication was used to compare effects of these substances on virus replication in Jurkat-tat cells. This coeff. was calcd. as the ratio of concns. of **HIV** p24 in supernatants to the amt. of viable cells. Muramylpeptides boosted **HIV** replication. Only one modified muramylpeptide .alpha.-butyl-MDP and tauroside H2 were not capable of boosting **HIV**-1 antigen prodn.

IT **53678-77-6**, Muramyldipeptide
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of Hedera taurica saponins and muramylpeptides on **HIV**-1 replication in lymphoblasts)

L64 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 1998 ACS
AN 1997:23840 HCAPLUS
DN 126:88052
TI Immunogenicity of **HIV**-1LAI gp160 and env peptides in squirrel monkey Saimiri sciureus using alumina and experimental adjuvants
AU Perraut, R.; Chouteau, P.; Moog, C.; Bonnemains, B.; Kieny, M. P.
CS Laboratoire d'Immunologie Parasitaire, Institut Pasteur de la Guyane Francaise, Cayenne, Fr. Guiana
SO Clin. Exp. Immunol. (1996), 106(3), 434-441

not correlate with protection. Immunization with a whole inactivated vaccine can protect primates from i.v. challenge with a monkey-cell grown cell-free **human immunodeficiency** virus type 2.

IT **53678-77-6**, Muramyl dipeptide
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(whole **HIV**-2 vaccines and adjuvants induce antibodies in cynomolgus monkeys)

L64 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 1998 ACS
AN 1992:39571 HCAPLUS
DN 116:39571
TI Native but not denatured recombinant **human immunodeficiency** virus type 1 gp120 generates broad-spectrum neutralizing antibodies in baboons
AU Haigwood, Nancy L.; Nara, Peter L.; Brooks, Eric; Van Nest, Gary A.; Ott, Gary; Higgins, Ketih W.; Dunlop, Nancy; Scandella, Carl J.; Eichberg, Jorg W.; Steimer, Kathelyn S.
CS Chiron Corp., Emeryville, CA, 94608-2916, USA
SO J. Virol. (1992), 66(1), 172-82
CODEN: JOVIAM; ISSN: 0022-538X
DT Journal
LA English
AB The protection of individuals from **human immunodeficiency** virus type 1 (**HIV**-1) infection with an envelope subunit derived from a single isolate will require the presentation of conserved epitopes in gp120. The objective here was to test whether a native recombinant gp120 (rgp120) immunogen would elicit responses to conserved neutralization epitopes that are not present in a denatured recombinant gp120 antigen from the same virus isolate. In a large study of baboons, the authors generated heterologous neutralizing activity with native, glycosylated rgp120SF2 but not with denatured, nonglycosylated env 2-3SF2. After repeated exposure to rgp120SF2 formulated with one of several adjuvants, virus isolates from the United States, the Caribbean, and Africa were neutralized. The timing of the immunization regimen and the choice of adjuvant affected the virus neutralization titers both quant. and qual. Evidently vaccination with native, glycosylated rgp120 from a single virus isolate, **HIV**-SF2, may elicit a protective immune response effective against geog. and sequentially distinct **HIV**-1 isolates.
IT **61136-12-7**
RL: BIOL (Biological study)
(neutralizing antibody formation to native recombinant envelope glycoprotein of **HIV**-SF2 virus in baboons response to)

=> d his l66-

(FILE 'HCAPLUS' ENTERED AT 09:07:57 ON 08 DEC 1998)
SEL HIT RN L64

FILE 'REGISTRY' ENTERED AT 09:11:34 ON 08 DEC 1998
L66 2 S E25-E26
L67 1 S L66 NOT L63

=> d ide can l67

REFERENCE 9: 116:39571

REFERENCE 10: 115:151287

=> d his 168-

```
     (FILE 'AIDSLINE' ENTERED AT 09:12:16 ON 08 DEC 1998)
L68           0 S L43
L69           1 S L44
L70           2 S MURABUTIDE OR MURAMETIDE
L71          38 S ACETYLMURAMYL-ALANYL-ISOGLUTAMINE/CT,CN
L72           1 S N-ACETYLMURAMYL-ALANYLGLUTAMINE-N-BUTYL ESTER/CT,CN
L73          38 S L69-L72
L74          37 S L32
L75           0 S L74 NOT L73
L76          38 S L73,L74

     FILE 'EMBASE' ENTERED AT 09:15:23 ON 08 DEC 1998
L77           0 S L43
L78          30 S L44
L79          61 S MURABUTIDE/CT OR MURAMETIDE/CT
L80          61 S L78,L79
L81           0 S L80 AND HIV
L82           0 S L80 AND AIDS
L83           4 S L80 AND IMMUNODEFICIEN?
                E HUMAN IMMUNODEFICIEN/CT
                E E4+ALL/CT
L84       32362 S E5+NT/CT
                E HUMAN IMMUNODEFICIEN/CT
                E E87+ALL/CT
L85       68908 S E6+NT/CT
L86           0 S L80 AND L84,L85
L87           1 S L83 AND HUMAN IMMUNODEFICIEN?

=> fil embase

FILE 'EMBASE' ENTERED AT 09:21:05 ON 08 DEC 1998
COPYRIGHT (C) 1998 Elsevier Science B.V.  All rights reserved.

 FILE COVERS 1974 TO 3 Dec 1998 (19981203/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d all l87


L87  ANSWER 1 OF 1  EMBASE  COPYRIGHT 1998 ELSEVIER SCI. B.V.
AN   94150769  EMBASE
TI   Liposomes, muramyl dipeptide derivatives, and nontoxic lipid a
     derivatives as adjuvants for human malaria vaccines.
AU   Hui G.S.N.
CS   Department of Tropical Medicine, Leahi Hospital, 3675 Kilauca
     Avenue, Honolulu, HI 96816, United States
SO   AM. J. TROP. MED. HYG., (1994) 50/4 SUPPL. (41-51).
     ISSN: 0002-9637  CODEN: AJTHAB
CY   United States
```

Ljungdahl-Stahle E; Pertel S S; Grishkovets V I; Zemlyakov A E; Wahren B
CS Department of Microbiology and Virology, Crimean Medical Institute, Ukraine.
SO VACCINE, (1997). Vol. 15, No. 12-13, pp. 1479-86.
Journal code: X6O. ISSN: 0264-410X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 97448354
EM 199712
AB Muramyl dipeptide (MDP), eight new lipophilic MDP derivatives (MDPs) and three purified saponins were evaluated for their ability to induce immune responses in mice immunized with HIV-1 envelope protein rgp160 and for their ability to influence the HIV-1 replication in vitro. Three of nine new synthetic MDP derivatives (beta-butyl-MDP, MTPO-26 and beta cholesteryl-MDP) and one saponin (Taurosid I) have been shown to induce strong humoral immune responses to HIV-1 envelope glycoproteins rgp160 and rgp120. Three substances (beta-butyl-MDP, MDP-cholyl and beta-G27-MDP) induced high levels of T-cell stimulation to HIV-1 rgp160. beta-butyl-MDP induced the strongest B- and T-cell responses to HIV-1 glycoproteins. Two substances (beta-butyl-MDP and Taurosid I) did not induce an enhancement of HIV-1 replication in vitro and can be considered as promising adjuvants.
CT Check Tags: Animal; Female; Male; Support, Non-U.S. Gov't
Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives
***Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology**
*Adjuvants, Immunologic: PD, pharmacology
*HIV-1: DE, drug effects
HIV-1: PH, physiology
Mice
Mice, Inbred BALB C
*Saponins: PD, pharmacology
*Virus Replication: DE, drug effects
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**
CN 0 (Adjuvants, Immunologic); 0 (Saponins)

L76 ANSWER 4 OF 38 AIDSLINE
AN 1997:14146 AIDSLINE
DN MED-97216825
TI [Effect of saponins from Hedera taurica Carr. and modified muramylpeptides on replication of human immunodeficiency virus in vitro].
Vlianie saponinov iz Hedera taurica Carr. i modifitsirovannykh muramilpeptidov na reproduktsiiu virusa immunodefitsita cheloveka in vitro.
AU Krivorutchenko IuL; Andronovskaia I B; Chirva VIa; Pertel' S S; Grishkovets V I; Zemliakov A E; Kur'ianov V O; Krivoshein IuS
SO VOPROSY VIRUSOLOGII, (1997). Vol. 42, No. 1, pp. 34-6.
Journal code: XL8. ISSN: 0507-4088.
CY RUSSIA: Russian Federation
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA Russian
SL English
OS MEDLINE 97216825

EM 199706
AB The effects of muramyldipeptide (MDP), several new MDP derivatives, and saponins derived from Hedera taurica Carr, on the in vitro replication of HIV-1 were studied. The coefficient of alteration of the rate of HIV replication was used to compare these reagents' effects on virus replication in Jurkat-tat cells. This coefficient was calculated as the ratio of concentrations of HIV p24 in supernatants to the amount of viable cells. Muramylpeptides boosted HIV replication. Only one modified muramylpeptide alpha-butyl-MDP and tauroside H2 were not capable of boosting HIV-1 antigen production.
CT Check Tags: Human
***Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology**
Culture Media
English Abstract
HIV Core Protein p24: AN, analysis
*HIV-1: DE, drug effects
HIV-1: PH, physiology
Jurkat Cells
*Plants: CH, chemistry
*Saponins: PD, pharmacology
*Virus Replication: DE, drug effects
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**
CN 0 (Culture Media); 0 (HIV Core Protein p24); 0 (Saponins)

L76 ANSWER 5 OF 38 AIDSLINE
AN 1996:2606 AIDSLINE
DN MED-96002631
TI Induction of a CD8+ cytotoxic T lymphocyte response to soluble antigen given together with a novel muramyl dipeptide adjuvant, N-acetyl-D-glucosaminyl-(beta 1-4)-N-acetylmuramyl-L-alanyl-D-isoglutamine (GMDP).
AU Hornung R L; Longo D L; Gowda V L; Kwak L W
CS Biological Carcinogenesis & Development Program, Program Resources, Inc./DynCorp, Frederick, MD, USA.
SO THERAPEUTIC IMMUNOLOGY, (1995). Vol. 2, No. 1, pp. 7-14.
Journal code: CCS. ISSN: 0967-0149.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 96002631
EM 199601
AB We have investigated the ability of the novel muramyl dipeptide, GMDP, to act as an adjuvant for the induction of ovalbumin (OVA)-specific, CD8+ cytotoxic T lymphocyte (CTL) responses. C57Bl/6 mice were twice immunized s.c. with 50 micrograms OVA emulsified with a squalane, L121 pluronic containing Tween-80 vehicle either with (STP-GMDP) or without (STP) GMDP. Splenic precursor CD8+ CTL activity against E.G7-OVA, but not against EL-4 parental targets was detected in STP-GMDP immunized mice after 5 days of in vitro re-stimulation with irradiated E.G7-OVA cells, while mice immunized with OVA in STP alone or OVA alone failed to demonstrate CTL activity. OVA emulsified in a microfluidized STP vehicle formulation without GMDP also elicited the E.G7-OVA precursor CTL. The ability of GMDP to induce a class I-restricted, CD8+ CTL response to a soluble protein antigen may have implications for the development of useful vaccines against viral pathogens or tumours against which CTL responses are desirable.

Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives
Adjuvants, Immunologic
Antibodies, Monoclonal
*Arthritis, Adjuvant: PA, pathology
*Cyclosporine: TO, toxicity
CD4-CD8 Ratio
Flow Cytometry
*Lymphocyte Subsets: DE, drug effects
Rats
Rats, Inbred Lew
Spleen: CY, cytology
*Spleen: DE, drug effects
Tarsus, Animal: PA, pathology
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 59865-13-3 (Cyclosporine); 78113-36-7 (romurtide)
CN 0 (Adjuvants, Immunologic); 0 (Antibodies, Monoclonal)

L76 ANSWER 7 OF 38 AIDSLINE
AN 1995:2784 AIDSLINE
DN MED-95042886
TI Synthesis of immunoadjuvant conjugates with HIV-derived peptide inducing peptide-specific antibody.
AU Maruyama Y; Kurimura M; Achiwa K
CS School of Pharmaceutical Sciences, University of Shizuoka, Japan.
SO CHEMICAL AND PHARMACEUTICAL BULLETIN, (1994). Vol. 42, No. 8, pp. 1709-11.
Journal code: CZP. ISSN: 0009-2363.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
FS MED
LA English
OS MEDLINE 95042886
EM 199502
CT Check Tags: Animal; Male
***Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives**
Acetylmuramyl-Alanyl-Isoglutamine: CS, chemical synthesis
Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
Adjuvants, Immunologic: CH, chemistry
*Adjuvants, Immunologic: CS, chemical synthesis
Adjuvants, Immunologic: PD, pharmacology
Amino Acid Sequence
Antibody Specificity
*AIDS Vaccines: IM, immunology
Chromatography, High Pressure Liquid
Enzyme-Linked Immunosorbent Assay
*HIV Antibodies: BI, biosynthesis
*HIV Envelope Protein gp120: IM, immunology
*HIV-1: IM, immunology
Mice
Mice, Inbred BALB C
Molecular Sequence Data
Molecular Weight
Peptide Fragments: CS, chemical synthesis
Peptide Fragments: IM, immunology
Vaccines, Synthetic: IM, immunology
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**
CN 0 (Adjuvants, Immunologic); 0 (AIDS Vaccines); 0 (HIV Antibodies); 0

(HIV Envelope Protein gp120); 0 (Peptide Fragments); 0 (Vaccines, Synthetic)

L76 ANSWER 8 OF 38 AIDSLINE
AN 1995:2734 AIDSLINE
DN MED-95052854
TI Clinical and immunologic responses to human immunodeficiency virus (HIV) type 1SF2 gp120 subunit vaccine combined with MF59 adjuvant with or without muramyl tripeptide dipalmitoyl phosphatidylethanolamine in non-HIV-infected human volunteers.
AU Kahn J O; Sinangil F; Baenziger J; Murcar N; Wynne D; Coleman R L; Steimer K S; Dekker C L; Chernoff D
CS AIDS Program, San Francisco General Hospital, CA 94110.
SO JOURNAL OF INFECTIOUS DISEASES, (1994). Vol. 170, No. 5, pp. 1288-91.
Journal code: IH3. ISSN: 0022-1899.
CY United States
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
FS MED; Abridged Index Medicus Journals; Priority Journals
LA English
OS MEDLINE 95052854
EM 199502
AB A phase 1 study of 42 non-human immunodeficiency virus type 1 (HIV)-infected volunteers was initiated to determine the safety and immunogenicity of an HIV subunit vaccine consisting of recombinant envelope gp120 derived from HIVSF2 (rgp120SF2) combined with a novel adjuvant, MF59, with or without the immunomodulator muramyl tripeptide dipalmitoyl phosphatidylethanolamine (MTP-PE). All injections contained adjuvant MF59, and subjects were grouped according to MTP-PE dose. Injections were given on days 0, 30, 180, and 365. The vaccine was well tolerated with limited local and systemic reactions. These immunizations induced rgp120SF2-specific binding antibodies that persisted > or = 24 weeks. After three immunizations, all subjects receiving the antigen developed neutralizing antibodies to HIVSF2, and serum from 67% of these subjects also cross-neutralized HIVMN. ELISA-reactive antibodies to the HIVSF2 V3 region and strong lymphoproliferative responses to HIVSF2 envelope proteins were detected in all rgp120SF2-immunized subjects.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
***Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives**
Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage
*Adjuvants, Immunologic: AD, administration & dosage
Adolescence
Adult
AIDS Vaccines: AD, administration & dosage
*AIDS Vaccines: IM, immunology
Double-Blind Method
HIV Antibodies: BL, blood
*HIV Envelope Protein gp120: IM, immunology
Immunization
Middle Age
*Phosphatidylethanolamines: AD, administration & dosage
*Polysorbates: AD, administration & dosage

Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage
Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
*Adjuvants, Immunologic
Adjuvants, Immunologic: AD, administration & dosage
AIDS Vaccines: AD, administration & dosage
*AIDS Vaccines: IM, immunology
Cytotoxicity, Immunologic
Drug Carriers
*Gene Products, env: IM, immunology
HIV Antibodies: BI, biosynthesis
*HIV-1: IM, immunology
Interleukin-7: AD, administration & dosage
*Interleukin-7: IM, immunology
Liposomes
Mice
Mice, Inbred C3H
Phosphatidylethanolamines: AD, administration & dosage
*Phosphatidylethanolamines: IM, immunology
Recombinant Proteins: AD, administration & dosage
Recombinant Proteins: IM, immunology
Specific Pathogen-Free Organisms
T-Lymphocytes, Cytotoxic: IM, immunology
Vaccines, Synthetic: AD, administration & dosage
Vaccines, Synthetic: IM, immunology
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 83461-56-7 (CGP 19835 A)
CN 0 (Adjuvants, Immunologic); 0 (AIDS Vaccines); 0 (Drug Carriers); 0 (Gene Products, env); 0 (HIV Antibodies); 0 (Interleukin-7); 0 (Liposomes); 0 (Phosphatidylethanolamines); 0 (Recombinant Proteins); 0 (Vaccines, Synthetic)

L76 ANSWER 10 OF 38 AIDSLINE
AN 1994:6961 AIDSLINE
DN MED-94235370
TI Immune responses induced by prototype vaccines for AIDS in rhesus monkeys.
AU Ohkawa S; Wilson L A; Larosa G; Javaherian K; Martin L N; Murphey-Corb M
CS Department of Microbiology, Tulane Regional Primate Research Center, Covington, Louisiana 70433.
NC NO1-AI-62560 (NIAID)
NO1-AI-15093 (NIAID)
P51-RR-00164 (NCRR)
+
SO AIDS RESEARCH AND HUMAN RETROVIRUSES, (1994). Vol. 10, No. 1, pp. 27-38.
Journal code: ART. ISSN: 0889-2229.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 94235370
EM 199408
AB A battery of assay systems was used to profile both humoral and cell-mediated immune responses induced by immunization with candidate vaccines consisting of recombinant simian immunodeficiency virus (SIV) glycoproteins rgp110 (nondenatured) with SAF-M adjuvant (gp110 + SAF-M) or rgp140 (denatured) with Freund's adjuvant (gp140

CN 0 (Antibodies, Viral); 0 (AIDS Vaccines); 0 (IgG); 0 (Polysorbates); 0 (Retroviridae Proteins); 0 (Syntex adjuvant formulation); 0 (SIV envelope protein gp110); 0 (Vaccines, Synthetic); 0 (Viral Envelope Proteins)

L76 ANSWER 11 OF 38 AIDSLINE
AN 1993:15331 AIDSLINE
DN ICA9-93335772
TI Effect of muramyl peptides on replication of human immunodeficiency virus in combination with antiretrovirals.
AU Masihi K N; Chedid L
CS Robert Koch Institute, Berlin, Germany.
SO Int Conf AIDS, (1993). Vol. 9, No. 1, pp. 494 (Abstract No. PO-B28-2154).
CY GERMANY: Germany, Federal Republic of
DT Abstract
FS ICA9
LA English
EM 199311
AB Efforts to improve the hematologic tolerance of AZT and related compounds have led to the application of CSFs. Immunomodulator MDP can enhance monocyte-macrophage CSF in serum, induce a proliferation of multipotential stem cells in the bone marrow and increase the numbers of granulocyte-macrophage progenitors in the spleen. MDP has been shown possess an inhibitory activity against HIV infection of CD4-positive cells. In the present study, the effect of the combination of MDPs with suboptimal doses of ddC, AZT and IFN-gamma, were investigated. A significant synergistic activity against HIV infection of U937 cells was obtained using MDP, muradimetide, or **murametide** in combination with a suboptimal dose of AZT, ddC or a low-activity dose of interferon-gamma. Surprising synergistic activity was obtained using muradimetide in combination with even an inactive dose of ddC.
CT Check Tags: Comparative Study; Human
***Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology**
*Adjuvants, Immunologic: PD, pharmacology
Drug Synergism
*HIV: DE, drug effects
HIV: PH, physiology
*Interferon Type II: PD, pharmacology
Monocytes: DE, drug effects
Monocytes: MI, microbiology
Tumor Cells, Cultured
*Virus Replication: DE, drug effects
*Zalcitabine: PD, pharmacology
*Zidovudine: PD, pharmacology
RN 30516-87-1 (Zidovudine); **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 7481-89-2 (Zalcitabine); 82115-62-6 (Interferon Type II)
CN 0 (Adjuvants, Immunologic)

L76 ANSWER 12 OF 38 AIDSLINE
AN 1993:12996 AIDSLINE
DN ICA9-93336304
TI Phase 1 study of an HIV-1 gp 120 vaccine combined with MF59 and with dose escalation of MTP-PE, in sero-negative adults.
AU Kahn J; Chernoff D; Sinangil F; Baenziger J; Murcar N; Steimer K
CS University of California San Francisco.
SO Int Conf AIDS, (1993). Vol. 9, No. 1, pp. 70 (Abstract No.

dosage
Acetylmuramyl-Alanyl-Isoglutamine: TO, toxicity
Adjuvants, Immunologic: AD, administration & dosage
Adjuvants, Immunologic: TO, toxicity
Adult
*AIDS Vaccines: TO, toxicity
Double-Blind Method
HIV Envelope Protein gp120: IM, immunology
*HIV Envelope Protein gp120: TO, toxicity
*HIV-1: IM, immunology
Phosphatidylethanolamines: AD, administration & dosage
Phosphatidylethanolamines: TO, toxicity
*Vaccines, Synthetic: TO, toxicity
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 83461-56-7 (CGP 19835 A)
CN 0 (Adjuvants, Immunologic); 0 (AIDS Vaccines); 0 (HIV Envelope Protein gp120); 0 (Phosphatidylethanolamines); 0 (Vaccines, Synthetic)

L76 ANSWER 15 OF 38 AIDSLINE
AN 1993:9242 AIDSLINE
DN MED-93301828
TI Effects of adjuvants and multiple antigen peptides on humoral and cellular immune responses to gp160 of HIV-1.
AU Levi M; Ruden U; Birx D; Loomis L; Redfield R; Lovgren K; Akerblom L; Sandstrom E; Wahren B
CS Department of Virology, National Bacteriological Laboratory, Stockholm, Sweden.
SO JOURNAL OF ACQUIRED IMMUNE DEFICIENCY SYNDROMES, (1993). Vol. 6, No. 8, pp. 855-64.
Journal code: JOF. ISSN: 0894-9255.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 93301828
EM 199309
AB The capacity of five different adjuvants, AlPO4, a muramyldipeptide formulation (MDP.TSL), Freund's adjuvant, immunostimulating complex and its matrix components to elicit humoral and cellular responses in rabbits immunized with the human immunodeficiency virus type 1 (HIV-1) envelope protein rgp160IIIB was compared. The highest antibody titers against gp160 and gp41/gp120 epitopes were seen with rgp160 in MDP.TSL or Freund's adjuvant, whereas the broadest responses were seen in rabbits immunized with rgp160 in matrix or MDP.TSL. The broadest spectrum of high-avidity antibodies was also induced by rgp160 in MDP.TSL. Neutralizing titers against HIV-1IIIB, low titers to HIV-1MN, and the most efficient inhibition of viral cell-to-cell spread was seen with rgp160 in MDP.TSL. The strongest and most persisting cellular responses were induced by rgp160 in AlPO4 or MDP.TSL. Using MDP.TSL as the adjuvant, we also improved the immune response against gp120 epitopes by boosting rgp160-primed rabbits with rgp160, multiple antigenic peptides (MAPs), or unconjugated peptides. The MAPs induced high neutralizing titers and were superior to rgp160 alone in inducing both humoral and cellular reactivity. MAPs are therefore strong candidates for inclusion into future HIV-1 vaccines.
CT Check Tags: Animal; Female
Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology

*Adjuvants, Immunologic: PD, pharmacology
Aluminum: PD, pharmacology
Amino Acid Sequence
Antibody Affinity
Freund's Adjuvant: PD, pharmacology
Gene Products, env: CH, chemistry
*Gene Products, env: IM, immunology
*HIV Antibodies: BI, biosynthesis
HIV Antigens: CH, chemistry
*HIV Antigens: IM, immunology
HIV Envelope Protein gp41: IM, immunology
*HIV-1: IM, immunology
Immunity, Cellular: DE, drug effects
Immunization
Immunization, Secondary
ISCOMs: IM, immunology
ISCOMs: PD, pharmacology
Lymphocyte Transformation: IM, immunology
Molecular Sequence Data
Peptide Fragments: CH, chemistry
Peptide Fragments: IM, immunology
Phosphates: PD, pharmacology
Protein Precursors: CH, chemistry
*Protein Precursors: IM, immunology
Rabbits
Recombinant Proteins: CH, chemistry
Recombinant Proteins: IM, immunology
T-Lymphocytes: IM, immunology
Virus Replication: IM, immunology

RN 13765-93-0 (aluminum phosphate); **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 7429-90-5 (Aluminum); 9007-81-2 (Freund's Adjuvant)

CN 0 (Adjuvants, Immunologic); 0 (Gene Products, env); 0 (HIV Antibodies); 0 (HIV Antigens); 0 (HIV Envelope Protein gp160); 0 (HIV Envelope Protein gp41); 0 (ISCOMs); 0 (Peptide Fragments); 0 (Phosphates); 0 (Protein Precursors); 0 (Recombinant Proteins)

L76 ANSWER 16 OF 38 AIDSLINE
AN 1993:8499 AIDSLINE
DN MED-93271840
TI SIV vaccine protection of rhesus monkeys.
AU Gardner M B; Carlson J R; Jennings M; Rosenthal A; Langlois A; Haynes B; Bolognesi D; Palker T J
CS Department of Medical Pathology, University of California, Davis.
SO BIOTECHNOLOGY THERAPEUTICS, (1991). Vol. 2, No. 1-2, pp. 9-19. Journal code: BNI. ISSN: 0898-2848.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 93271840
EM 199309
AB Rhesus macaques (M. mulatta), immunized with an inactivated whole SIVmac vaccine and muramyl dipeptide or Freund's incomplete adjuvant, were protected against IV challenge infection with 10 animal infectious doses of the homologous virus. The protection in these animals appeared to be complete, with no breakthrough of latent virus infection over a 10-month period. Vaccine protection in this model was correlated generally with a high level of SIVmac

envelope antibody by ELISA and immunoblot, high titers of syncytial inhibiting antibody, and, more specifically, with the presence of antibodies binding to a putative V3 loop synthetic peptide of the SIVmac outer envelope. This model can now be used for further identification of the protective epitopes and protective host immune responses as well as for development of novel and better AIDS vaccines.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage
Antibodies, Viral: BI, biosynthesis
Antigens, Viral
Freund's Adjuvant: AD, administration & dosage
Gene Products, env: IM, immunology
Macaca mulatta
Neutralization Tests
Retroviridae Proteins, Oncogenic: IM, immunology
*Simian Acquired Immunodeficiency Syndrome: PC, prevention & control
*SIV: IM, immunology
Vaccines, Inactivated: AD, administration & dosage
Vaccines, Inactivated: PD, pharmacology
Viral Vaccines: AD, administration & dosage
*Viral Vaccines: PD, pharmacology

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 9007-81-2 (Freund's Adjuvant)

CN 0 (simian immunodeficiency virus transmembrane protein); 0 (Antibodies, Viral); 0 (Antigens, Viral); 0 (Gene Products, env); 0 (Retroviridae Proteins, Oncogenic); 0 (Vaccines, Inactivated); 0 (Viral Vaccines)

L76 ANSWER 17 OF 38 AIDSLINE
AN 1993:2935 AIDSLINE
DN MED-93103854
TI Comparison of protection afforded by whole virus ISCOM versus MDP adjuvanted formalin-inactivated SIV vaccines from IV cell-free or cell-associated homologous challenge.
AU Osterhaus A; de Vries P; Morein B; Akerblom L; Heeney J
CS Laboratory of Immunobiology, National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands.
SO AIDS RESEARCH AND HUMAN RETROVIRUSES, (1992). Vol. 8, No. 8, pp. 1507-10.
Journal code: ART. ISSN: 0889-2229.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED: Priority Journals
LA English
OS MEDLINE 93103854
EM 199303
AB A SIV-ISCOM and a SIV-MDP adjuvanted vaccine were tested for their potential to induce protection from intravenous cell-free or cell-associated homologous SIV challenge in rhesus monkeys (Macaca mulatta). Seven monkeys vaccinated four times over a four-month period with either the SIV-ISCOM or the SIV-MDP vaccine were challenged intravenously with approximately 10 MID50 cell-free SIVmac251 (32H). They all were protected from developing viremia during a three-month observation period. Two other groups of four monkeys were vaccinated essentially in the same way with either of these vaccines. They were challenged intravenously with approximately 10 MID50 of infected PBMC of a rhesus monkey that had

been infected with SIVmac251 (32H) 11 months earlier (stock prepared by J. Heeney). Two monkeys of each of these two groups proved to be protected from developing viremia during a two-month observation period. For both the cell-free and the cell-associated SIV challenge, monkeys vaccinated with measles virus ISCOMS or MDP adjuvanted measles virus antigen, served as controls. They all became viremic within two weeks after SIV challenge. This is the first demonstration that vaccinated previously unchallenged nonhuman primates can be protected from infection with lentivirus-infected PBMC from another animal. Serological analysis indicated that SIV-specific serum antibody titers were considerably higher in SIV-ISCOM vaccinated animals than in the SIV-MDP vaccinated animals. The serology also confirmed the protection data, by showing the absence of increase in SIV-specific serum antibodies in apparently protected animals after challenge.

CT Check Tags: Animal; Comparative Study; Support, Non-U.S. Gov't
***Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology**
*Adjuvants, Immunologic
Antibodies, Viral: BI, biosynthesis
*ISCOMs: IM, immunology
Lymphocytes: MI, microbiology
Lymphocytes: TR, transplantation
Macaca mulatta: IM, immunology
*Simian Acquired Immunodeficiency Syndrome: PC, prevention & control
Simian Acquired Immunodeficiency Syndrome: TM, transmission
*SIV: IM, immunology
SIV: IP, isolation & purification
*Vaccines, Inactivated: IM, immunology
*Viral Vaccines: IM, immunology

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**

CN 0 (Adjuvants, Immunologic); 0 (Antibodies, Viral); 0 (ISCOMs); 0 (Vaccines, Inactivated); 0 (Viral Vaccines)

L76 ANSWER 18 OF 38 AIDSLINE

AN 1993:2550 AIDSLINE

DN MED-93090458

TI The control of the antibody isotype response to recombinant human immunodeficiency virus gp120 antigen by adjuvants.

AU Bomford R; Stapleton M; Winsor S; McKnight A; Andronova T

CS Wellcome Research Laboratories, Beckenham, Kent, England.

SO AIDS RESEARCH AND HUMAN RETROVIRUSES, (1992). Vol. 8, No. 10, pp. 1765-71.
Journal code: ART. ISSN: 0889-2229.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

FS MED; Priority Journals

LA English

OS MEDLINE 93090458

EM 199303

AB Both saponin and muramyl dipeptide (MDP) formulated with a squalane-in-water emulsion of large particle size prepared with a vortex mixer were superior to Al(OH)3 as adjuvants for HIV gp120 in mice. All the adjuvants induced IgG1 antibody, but saponin elicited the highest titers of IgG2a. The secretion of interleukin-5 (IL-5) and interferon gamma (IFN gamma) by lymph node cells cultured in vitro with gp120 was studied. All the cultures secreted IL-5, but only those from saponin-immunized mice produced IFN gamma, suggesting that saponin is capable of activating both the Th1 and TH2 T-cell subsets. The titers of neutralizing antibodies were low

with both MDP and saponin, and they occurred in mice which were also positive for antibodies against a V3 loop peptide. Glucosaminylmuramyl dipeptide (GMDP) which is less pyrogenic than MDP and a nonpyrogenic analog GMDPA, displayed equivalent adjuvant activity to MDP. The level and isotype composition of antibodies induced by GMDP in combination with squalane emulsions depended on the dimension of the emulsion particles. With a large (2500 nm) particle size the response was confined to IgG1 in Balb/c mice, but when this was reduced to 150 nm by sonication the antibody response was increased and relatively high levels of IgG2a appeared in some mice.

CT Check Tags: Animal; Comparative Study; Female; Male; Support, Non-U.S. Gov't
Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage
Adjuvants, Immunologic: AD, administration & dosage
Aluminum Hydroxide: AD, administration & dosage
*HIV Antibodies: BI, biosynthesis
HIV Envelope Protein gp120: AD, administration & dosage
*HIV Envelope Protein gp120: IM, immunology
*Immunoglobulin Isotypes: BI, biosynthesis
Interferon Type II: SE, secretion
Interleukin-5: SE, secretion
Mice
Mice, Inbred BALB C
Mice, Inbred CBA
Particle Size
Poloxalene: AD, administration & dosage
Recombinant Proteins: AD, administration & dosage
Recombinant Proteins: IM, immunology
Saponins: AD, administration & dosage

RN 21645-51-2 (Aluminum Hydroxide); **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 82115-62-6 (Interferon Type II); 9003-11-6 (Poloxalene)

CN 0 (Adjuvants, Immunologic); 0 (HIV Antibodies); 0 (HIV Envelope Protein gp120); 0 (Immunoglobulin Isotypes); 0 (Interleukin-5); 0 (Recombinant Proteins); 0 (Saponins)

L76 ANSWER 19 OF 38 AIDSLINE
AN 1993:1447 AIDSLINE
DN MED-93047471
TI Selection of a muramyl peptide based on its lack of activation of nuclear factor-kappa B as a potential adjuvant for AIDS vaccines.
AU Schreck R; Bevec D; Dukor P; Baeuerle P A; Chedid L; Bahr G M
CS Laboratorium fur Molekulare Biologie, Ludwig-Maximilians-Universitat, Martinsried, Germany.
SO CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1992). Vol. 90, No. 2, pp. 188-93.
Journal code: DD7. ISSN: 0009-9104.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals; Cancer Journals
LA English
OS MEDLINE 93047471
EM 199302
AB Activation of the cellular transcription factor nuclear factor-kappa B (NF-kappa B) by cytokines and other immunostimulants has been tightly linked with enhanced replication of human immunodeficiency virus-type 1 (HIV-1) in infected cells. Various immunomodulators are

L76 ANSWER 24 OF 38 AIDSLINE
AN 1992:8223 AIDSLINE
DN MED-92287545
TI Impaired stimulation of anti-bovine serum albumin IgG antibodies by vaccine adjuvants in murine acquired immunodeficiency syndrome.
AU Phillips N C
CS Montreal General Hospital Research Institute, Quebec, Canada.
SO FEMS MICROBIOLOGY IMMUNOLOGY, (1992). Vol. 4, No. 4, pp. 209-18. Journal code: AO3. ISSN: 0920-8534.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 92287545
EM 199209
AB The effect of three adjuvants - alum, N-acetylmuramyl-L-alanyl-D-isoglutamine (MDP), and liposomes - on the IgG antibody isotype response to bovine serum albumin (BSA), was determined in normal and LP-BM5 retrovirus infected C57BL/6 mice. Alum and MDP induced comparable levels of IgG antibodies in normal mice (predominantly IgG1 (greater than 90%)), whereas liposomes induced IgG1 (60%), IgG2a/b (30%) and IgG3 (10%) antibodies. IgG antibody levels using liposomes as adjuvant were five-fold higher than those observed with alum or MDP. Immunization after LP-BM5 infection significantly reduced the effectiveness of alum and MDP, IgG antibody levels being reduced by 80 and 90% at 3 or 7 weeks respectively. The adjuvant activity of liposomes was reduced by 55 and 65% when immunization was started 3 or 7 weeks post LP-BM5 infection. Boosting of pre-immune mice with BSA and alum, MDP or liposomes 3 weeks after LP-BM5 infection showed that, while the magnitude of the antibody response and isotype distribution was not affected, the persistence of the response was severely diminished compared to control, non-infected mice. The reduced immunoadjuvant activity correlated with a reduction in the frequency of splenic Thy1.2+/CD4+ T cells. These results demonstrated that liposomes were more effective than alum or MDP in inducing IgG antibodies, and that immunoadjuvant activity for prophylactic or therapeutic immunization for all 3 adjuvants was significantly impaired by retroviral infections.
CT Check Tags: Animal; Comparative Study; Female
Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology
*Adjuvants, Immunologic: PD, pharmacology
Alum Compounds: PD, pharmacology
*IgG: BI, biosynthesis
Immunoglobulin Isotypes: BI, biosynthesis
Immunologic Memory
Liposomes: IM, immunology
Mice
Mice, Inbred C57BL
*Murine Acquired Immunodeficiency Syndrome: IM, immunology
Serum Albumin, Bovine: IM, immunology
T-Lymphocyte Subsets: IM, immunology
RN 10043-01-3 (aluminum sulfate); **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**
CN 0 (Adjuvants, Immunologic); 0 (Alum Compounds); 0 (IgG); 0 (Immunoglobulin Isotypes); 0 (Liposomes); 0 (Serum Albumin, Bovine)

L76 ANSWER 25 OF 38 AIDSLINE
AN 1992:6924 AIDSLINE

DN PRIM9-1680292
TI Vaccine protection of rhesus macaques against SIVmac infection by high but not low doses of inactivated whole SIVmac immunogen.
AU Hartung S; Norley S; Bourquin P; Ennen J; Kurth R
CS Paul-Ehrlich-Institut, Paul-Ehrlich-Str. 51 - 59, 6070 Langen.
SO Symp Nonhum Primate Models AIDS, (1991). Vol. 9, pp. 121 (Abstract No. 102).
CY United States
DT Abstract
FS PRIM9
LA English
EM 199208
AB Eight Rhesus macaques were immunized intramuscularly four times (0, 1, 2, 4 months) over a period of 4 months with a formalin inactivated whole SIV vaccine in the presence of muramyl dipeptide (MDP) as adjuvant. Four animals received 0.5 mg and the other four 0.1 mg immunogen per injection. Three weeks after the final immunization the vaccinated monkeys along with two control monkeys were challenged intravenously with 10-50 MID50 of SIVmac251-32H. At the time of challenge 3 out of 4 animals of the high dose group has high titers (greater than 1:400) of antibody able to neutralize in vitro the homologous 32H strain of SIVmac. All other animals had low but measurable titers (1:50 - 1:200) of neutralizing antibody. The status of other immune parameters will be presented. Upon challenge three of the four animals from the low dose group (plus the nonvaccinated control animals) became infected as demonstrated by reisolation of virus from PBMC taken at two weeks post challenge and the development of a strong anamnestic response to SIVmac antigen. All other animals (one from low dose group and all four of the high dose group) remain negative by both parameters. These data indicate that when used in conjunction with MDP, the amount of immunogen required per immunization is between 0.1 and 0.5 mg. In addition, there is no apparent correlation between protection and the levels of homologous neutralizing antibody.
CT Check Tags: Animal
Acetylmuramyl-Alanyl-Isoglutamine: AD, administration & dosage
Antibodies, Viral: AN, analysis
Antigens, Viral: IM, immunology
Macaca mulatta
Neutralization Tests
*SIV: IM, immunology
*Vaccines, Inactivated: AD, administration & dosage
*Vaccines, Synthetic: AD, administration & dosage
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**
CN 0 (Antibodies, Viral); 0 (Antigens, Viral); 0 (Vaccines, Inactivated); 0 (Vaccines, Synthetic)

L76 ANSWER 26 OF 38 AIDSLINE
AN 1992:4566 AIDSLINE
DN MED-92182252
TI Adjuvant formulations and their mode of action.
AU Allison A C; Byars N E
CS Syntech Research, Palo Alto, CA 94304.
SO SEMINARS IN IMMUNOLOGY, (1990). Vol. 2, No. 5, pp. 369-74.
Journal code: A61. ISSN: 1044-5323.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals

LA English
OS MEDLINE 92182252
EM 199206
AB We have developed an adjuvant formulation (SAF) consisting of a synthetic muramyl dipeptide analogue (N-acetylmuramyl-L-threonyl-D-isoglutamine) in a squalane-Pluronic polymer emulsion. Used with a variety of antigens SAF elicits cell-mediated immunity and antibodies of protective isotypes (IgG2a in the mouse). SAF augments responses to influenza virus haemagglutinin and hepatitis B virus surface antigen. Vaccines using SAF have protected guinea pigs against genital herpes simplex virus infections and subhuman primates against Epstein-Barr virus and simian immunodeficiency virus infections. Properties of SAF are compared with those of other adjuvants, including lipopolysaccharide analogs, ISCOMs and liposomes.
CT Check Tags: Animal
***Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives**
Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
*Adjuvants, Immunologic
Adjuvants, Immunologic: CH, chemistry
*Antigens, Viral: IM, immunology
Emulsions
Guinea Pigs
Haplorhini
Hepatitis B Virus: IM, immunology
Herpesvirus 4, Human: IM, immunology
Immunity, Cellular
*Immunotherapy, Active
Mice
Orthomyxoviridae: IM, immunology
Simplexvirus: IM, immunology
SIV: IM, immunology
*Vaccines: IM, immunology
RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 66112-59-2 (N-acetylmuramyl-threonyl-isoglutamine)
CN 0 (Adjuvants, Immunologic); 0 (Antigens, Viral); 0 (Emulsions); 0 (Vaccines)

L76 ANSWER 27 OF 38 AIDSLINE
AN 1991:4933 AIDSLINE
DN MED-91175188
TI Vaccine protection of rhesus macaques against simian immunodeficiency virus infection.
AU Carlson J R; McGraw T P; Keddie E; Yee J L; Rosenthal A; Langlois A J; Dickover R; Donovan R; Luciw P A; Jennings M B; et al
CS Department of Pathology, School of Medicine, University of California, Davis 95616.
NC AI25900 (NIAID)
AI26471 (NIAID)
SO AIDS RESEARCH AND HUMAN RETROVIRUSES, (1990). Vol. 6, No. 11, pp. 1239-46.
Journal code: ART. ISSN: 0889-2229.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 91175188
EM 199107

glycoprotein (gp31). Protected monkeys tended to have higher titers of syncytial inhibition antibody prior to challenge. An anamnestic response after challenge was observed only in the vaccinated monkeys that became infected. Vaccinated animals that became challenge-infected tended to live longer than infected controls. These results confirm those at other primate centers and indicate that killed whole SIV vaccines can protect against low challenge doses of SIV and prevent early death in those monkeys that do become infected. The mechanism of this protection remains undetermined. Initial results from a cross-challenge experiment done in collaboration with Dr. Murphey-Corb (Delta Regional Primate Research Center) indicate that SIVmac immunized monkeys are protected against IV challenge with 10 ID of SIVsm and, conversely, SIVsm immunized monkeys are protected against IV challenge with 10 ID of SIVmac. These two SIV strains differ by about 17% in envelope sequences indicating that the vaccine induced protection appears to be fairly broad. These findings add optimism to the possibility of an eventual AIDS vaccine.

CT Check Tags: Animal
***Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology**
Antibodies, Viral: BI, biosynthesis
Cells, Cultured
Dose-Response Relationship, Immunologic
*Freund's Adjuvant
Leukocytes, Mononuclear: MI, microbiology
Macaca mulatta
*Simian Acquired Immunodeficiency Syndrome: PC, prevention & control
SIV: GD, growth & development
*SIV: IM, immunology
Viral Envelope Proteins: IM, immunology
*Viral Vaccines
Virus Activation: IM, immunology

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 9007-81-2 (Freund's Adjuvant)

CN 0 (Antibodies, Viral); 0 (Viral Envelope Proteins); 0 (Viral Vaccines)

L76 ANSWER 31 OF 38 AIDSLINE
AN 1991:3441 AIDSLINE
DN MED-91108143
TI Safety and immunogenicity of a genetically engineered human immunodeficiency virus vaccine.
AU Wintsch J; Chaignat C L; Braun D G; Jeannet M; Stalder H; Abrignani S; Montagna D; Clavijo F; Moret P; Dayer J M; et al
CS Department of Medicine, University Hospital, Geneva, Switzerland.
NC AI-22778 (NIAID)
SO JOURNAL OF INFECTIOUS DISEASES, (1991). Vol. 163, No. 2, pp. 219-25. Journal code: IH3. ISSN: 0022-1899.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
FS MED; Abridged Index Medicus Journals; Priority Journals
LA English
OS MEDLINE 91108143
EM 199105
AB A phase 1 trial of a candidate human immunodeficiency virus type 1 (HIV-1) vaccine was done in 25 healthy seronegative subjects. The antigen, env2-3 (SF2), was a nonglycosylated polypeptide representing the gp120 region of the env gene of the HIV-1(SF2)

isolate. It was produced in genetically engineered yeast as a denatured molecule incapable of binding CD4. A synthetic lipophilic muramyl tripeptide (MTP-PE) was used as an adjuvant. Ten subjects received adjuvant alone and 15 received 50- or 250-micrograms doses of env2-3 (SF2) administered intramuscularly in two immunization regimens. In general, adjuvant and vaccine were well tolerated. Antibody responses to both the homologous antigen, env2-3 (SF2), and antigens from other highly divergent HIV isolates were elicited in the majority of vaccine recipients. However, antibody titers were low, without neutralizing activity. In 9 of 11 subjects who received the complete vaccine immunization series, a significant specific T lymphocyte response was observed.

CT Check Tags: Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives
Acetylmuramyl-Alanyl-Isoglutamine: AE, adverse effects
Acetylmuramyl-Alanyl-Isoglutamine: IM, immunology
Adjuvants, Immunologic: AE, adverse effects
Adult
Antiviral Agents: AE, adverse effects
Antiviral Agents: IM, immunology
Blotting, Western
Drug Evaluation
Drug Tolerance
Enzyme-Linked Immunosorbent Assay
HIV Antibodies: BI, biosynthesis
HIV Envelope Protein gp120: IM, immunology
*HIV-1: IM, immunology
Immunoblotting
Leukocytes, Mononuclear: IM, immunology
Lymphocyte Transformation
Middle Age
Phosphatidylethanolamines: AE, adverse effects
Phosphatidylethanolamines: IM, immunology
T-Lymphocytes: IM, immunology
Vaccines, Synthetic: AE, adverse effects
Vaccines, Synthetic: IM, immunology
Viral Vaccines: AE, adverse effects
*Viral Vaccines: IM, immunology

RN **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**; 83461-56-7 (CGP 19835 A)

CN 0 (Adjuvants, Immunologic); 0 (Antiviral Agents); 0 (HIV Antibodies); 0 (HIV Envelope Protein gp120); 0 (Phosphatidylethanolamines); 0 (Vaccines, Synthetic); 0 (Viral Vaccines)

L76 ANSWER 32 OF 38 AIDSLINE
AN 1991:1828 AIDSLINE
DN MED-91069612
TI The lipophilic muramyl peptide MTP-PE is a potent inhibitor of HIV replication in macrophages.
AU Lazdins J K; Woods-Cook K; Walker M; Alteri E
CS CIBA-GEIGY Limited Basel, Pharma Research Laboratories, Switzerland.
SO AIDS RESEARCH AND HUMAN RETROVIRUSES, (1990). Vol. 6, No. 10, pp. 1157-61.
Journal code: ART. ISSN: 0889-2229.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

AB OBJECTIVE: To develop adjuvant formulations suitable for human vaccine use that surpass alum in their ability to enhance immunity to HIV-1 subunit immunogens. METHODS: A series of adjuvant formulations consisting of MTP-PE in metabolizable oil emulsions have been compared to conventional adjuvants such as alum and Freund's. Experimental animals were immunized with recombinant HIV-1 gp120 antigens (both non-glycosylated denatured and fully glycosylated native versions) in the various formulations, their sera were tested for ELISA-reactive and virus neutralizing antibodies and their helper T cell responses were assessed by lymphoproliferative assays. RESULTS: Most of these novel adjuvant formulations were effective in guinea pigs, mice and rabbits. However, the properties of the emulsion dramatically influenced the efficacy of these formulations in larger animals such as goats and baboons. One new formulation was as effective as Freund's incomplete adjuvant and was also at least 10-fold more effective than alum in enhancing antibody responses, neutralizing antibody titers and lymphoproliferative responses to recombinant gp120 antigens in large animals. CONCLUSIONS: Improved adjuvants with the potential of enhancing immune responses to recombinant HIV-1 gp120 antigens in humans have been developed. Further immunogenicity studies and extensive safety trials with these formulations are in progress.

CT Check Tags: Animal
Acetylmuramyl-Alanyl-Isoglutamine: AA, analogs & derivatives
Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology
*Adjuvants, Immunologic
*HIV Antibodies: BI, biosynthesis
*HIV Envelope Protein gp120: IM, immunology
*HIV-1: IM, immunology
Immunization
*Recombinant Proteins: IM, immunology

RN 64374-58-9 (muramyl tripeptide)

CN 0 (Adjuvants, Immunologic); 0 (HIV Antibodies); 0 (HIV Envelope Protein gp120); 0 (Recombinant Proteins)

L76 ANSWER 34 OF 38 AIDSLINE

AN 1990:7260 AIDSLINE

DN MED-90253926

TI Muramyl dipeptide inhibits replication of human immunodeficiency virus in vitro.

AU Masihi K N; Lange W; Rohde-Schulz B; Chedid L

CS Robert Koch Institute, Federal Health Office, West Berlin, Germany.

SO AIDS RESEARCH AND HUMAN RETROVIRUSES, (1990). Vol. 6, No. 3, pp. 393-9.
Journal code: ART. ISSN: 0889-2229.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

FS MED; Priority Journals

LA English

OS MEDLINE 90253926

EM 199008

AB In the search for compounds capable of inducing endogenous production of colony-stimulating factor (CSF) and possessing activity against human immunodeficiency virus (HIV), an immunomodulator, muramyl dipeptide (MDP), was investigated. MDP can enhance monocyte-macrophage CSF in serum and promote nonspecific resistance against a variety of microbial pathogens. MDP exhibited an inhibitory activity against HIV infection of CD4+ H9 lymphocytes

and U937 monocytoid cells. An inhibitor of viral reverse transcriptase, 2', 3'-dideoxyadenosine, produced potent inhibition in cultures which were similarly infected with HIV. MDP could partially reduce antigen production in persistently HIV-infected KE37/1 lymphocyte cultures.

CT Check Tags: Human
***Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology**
Cells, Cultured
Colony-Stimulating Factors: BI, biosynthesis
Dideoxyadenosine: PD, pharmacology
Gene Products, gag: BI, biosynthesis
*HIV: DE, drug effects
HIV: GD, growth & development
Viral Core Proteins: BI, biosynthesis
*Virus Replication: DE, drug effects

RN 4097-22-7 (Dideoxyadenosine); **53678-77-6 (Acetylmuramyl-Alanyl-Isoglutamine)**

CN 0 (Colony-Stimulating Factors); 0 (Gene Products, gag); 0 (HIV Core Protein p24); 0 (Viral Core Proteins)

L76 ANSWER 35 OF 38 AIDSLINE
AN 1990:3642 AIDSLINE
DN MED-90155807
TI Exacerbation of human immunodeficiency virus infection in promonocytic cells by bacterial immunomodulators.
AU Masihi K N; Lange W; Rohde-Schulz B
CS Robert Koch Institute, Federal Health Office, Berlin, F.R.G.
SO JOURNAL OF ACQUIRED IMMUNE DEFICIENCY SYNDROMES, (1990). Vol. 3, No. 3, pp. 200-5.
Journal code: JOF. ISSN: 0894-9255.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 90155807
EM 199005
AB Common bacterial infections are increasingly being diagnosed in HIV-infected individuals. Cells of the monocyte-macrophage lineage kill invading bacterial pathogens and subsequently release immunoadjuvant components from the degraded cell walls. Since monocytes can be infected with HIV, effects of bacterial immunomodulators on infected promonocytic U937 cells were investigated. Synthetic muramyl peptide, mycobacterial trehalose dimycolate, and detoxified endotoxin exhibited an initial reduction followed by a rapid increase in HIV p24 antigen production. The upregulation of virus expression was correlated with enhanced interleukin-1 beta levels and a decrease in TNF-alpha production.

CT Check Tags: Human
***Acetylmuramyl-Alanyl-Isoglutamine: PD, pharmacology**
Cell Line
*Cord Factors: PD, pharmacology
Dideoxyadenosine: PD, pharmacology
*Glycolipids: PD, pharmacology
HIV-1: DE, drug effects
*HIV-1: PH, physiology
Interferon Type II: PD, pharmacology
Interleukin-1: BI, biosynthesis
*Lipid A: AA, analogs & derivatives
Lipid A: PD, pharmacology

Blood, Blood-Forming Organs and Body Fluids-Lymphatic Tissue and Reticuloendothelial System *15008
Pharmacology-Immunological Processes and Allergy *22018
Immunology and Immunochemistry-Immunopathology, Tissue Immunology *34508
Medical and Clinical Microbiology-Virology *36006
Chemotherapy-Antiviral Agents *38506
BC **Retroviridae 02623**

=> d all l4 2

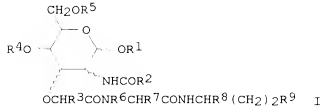
L4 ANSWER 2 OF 2 BIOSIS COPYRIGHT 1998 BIOSIS
AN 96:361435 BIOSIS
DN 99083791
TI Enhancement by muramyl peptides of the protective response of interferon-alpha-beta against encephalomyocarditis virus infection.
AU Pouillart P R; Audibert F M; Chedid L A; LeFrancier P L; Bahr G M
CS VACSYN S.A., 33 Boulevard du General Martial Valin, 75015 Paris, France
SO International Journal of Immunopharmacology 18 (3). 1996. 183-192. ISSN: 0192-0561
LA English
PR Biological Abstracts Vol. 102 Iss. 004 Ref. 049240
AB The use of interferon-alpha (IFN-alpha) in the treatment of infectious diseases has shown limited efficacy and dose-limiting toxicity. We have selected safe immunomodulators of the muramyl peptide family with the potential of enhancing the efficacy of IFN-alpha without resulting in increased toxicity. One of these synthetic muramyl dipeptide (MDP) derivatives, namely **murabutide** which is in a clinical stage of development, has been recently found to synergize with IFN-alpha-2a in the selective induction of anti-inflammatory mediators and to enhance the biological activities of the therapeutic cytokine. The present study was performed to assess the antiviral activity of such muramyl peptides and a possible potentiation of the antiviral activity of IFN-alpha/beta by associated therapy using the classical assay of Encephalomyocarditis virus (EMCV) infection. In vitro, pretreatment of Moloney Sarcoma virus (MSV)-transformed cell line with MDP derivatives followed by treatment with IFN-alpha/beta showed a synergistic protection against the cytopathogenic effect of a subsequent EMCV infection. None of the MSV cultures could be protected by stimulation with muramyl peptides alone. In vivo, all of the muramyl peptide derivatives tested were found to be more potent than the parent molecule MDP in inducing protection against death or in the prolongation of the mean survival time of infected mice. Sequential administration of suboptimal doses of exogenous IFN-alpha/beta and muramyl peptides established a strong antiviral state and considerably improved the protective effect of the cytokine, frequently leading to an abortive infection. Our findings suggest that combination therapy with safe muramyl peptides and IFN-alpha/beta could constitute a highly effective and new regimen for the treatment of viral infections in humans.
ST RESEARCH ARTICLE; MOUSE; **MURABUTIDE**; IMMUNOLOGIC-DRUG; MOLONEY SARCOMA VIRUS; INTERFERON-ALPHA; ANTIVIRAL-DRUG; HORMONE-DRUG; INTERFERON-BETA; ANTIVIRAL-DRUG; HORMONE-DRUG; CYTOKINE; TOXICITY; POTENTIAL CLINICAL APPLICATION
RN **74817-61-1** (MURABUTIDE)
CC Biochemical Studies-Proteins, Peptides and Amino Acids 10064

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as drug for enhancing host resistance against opportunistic infections in **AIDS** patients)

L62 ANSWER 21 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1990:112072 HCAPLUS
DN 112:112072
TI Dipeptidyl saccharides as host resistance enhancers in **AIDS** -immuno-compromised hosts and methods of use
IN Durette, Philippe L.
PA Merck and Co., Inc., USA
SO U.S., 19 pp.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4866035	A	19890912	US 87-105056	19871005

PI US 4866035
OS MARPAT 112:112072
GI



I

AB The dipeptidylsaccharides I [R1 = H, (un)substituted alkyl, alkoxy, etc.; R2 = (un)substituted alkyl, alkoxy, alkylmercapto, etc.; R3 = H, alkyl; R4, R5 = H, alkanoyl, benzoyl, naphthoyl, etc.; R6 = H; R6R7 = CH2CH2CH2; R8, R9 = CO2H, alkoxycarbonyl, (un)substituted CONH2, etc.] are prepd. as agents for enhancing host resistance to opportunistic bacterial, viral or fungal infections in **AIDS** patients. I help to suppress the **AIDS** virus infection itself. A soln. of benzyl 2-acetamido-4,6-O-benzylidene-2-deoxy-3-O-(D-2-propionyl-L-alanyl-D-isoglutamine benzyl ester)-.alpha.-D-galactopyranoside (prepn. given) in HOAc was hydrogenolyzed over Pd black, to give 2-acetamido-2-deoxy-3O-(D-2-propionyl-L-alanyl-D-isoglutamine)-D-galactose. I (no specific compd. given), injected i.p., at 100-300 mg/kg, to mice immunized with BSA (bovine serum albumin), increased the prodn. of anti-BSA antibodies. I may be administered jointly with known antiviral anti-**AIDS** drugs, such as azidothymidine, ansamycin, ribavirin, etc.

IT **69351-74-2P 75283-22-6P 75283-24-8P**
76465-71-9P 76497-96-6P 76498-00-5P
87420-93-7P 125637-73-2P 125637-74-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as host resistance enhancer, in **AIDS**)

L62 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1987:605162 HCAPLUS
DN 107:205162

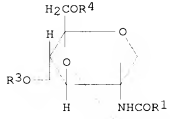
lymphocyte cultures.

IT **53678-77-6**, Muramyl dipeptide
RL: BIOL (Biological study)
(**human immunodeficiency** virus replication in infected cells inhibition by)

L62 ANSWER 20 OF 23 HCAPLUS COPYRIGHT 1998 ACS
AN 1990:112074 HCAPLUS
DN 112:112074
TI Preparation of dipeptidyl-2-amino-1,2-dideoxy-D-glucose derivatives as host resistance enhancers in **AIDS**-immunocompromised hosts and methods of use
IN Durette, Philippe L.
PA Merck and Co., Inc., USA
SO U.S., 11 pp.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 4868157	A	19890919	US 87-105051	19871005

GI



$R^2CHCONR^5CHR^6CONHCHR^7(CH_2)_2R^8$ I

AB The title compds. [R1 = (un)substituted alkyl or Ph; R2 = H, alkyl; R3, R4 = H, acyl, R11(CO)nX(CR9R10)mCO; R5 = H; R6 = H, alkyl, HOCH2, HSCH2, (un)substituted benzyl; R5R6 = (CH2)3; R7, R8 = CO2H, alkoxycarbonyl, (un)substituted CONH2; R9R10 = H, alkyl, alkenyl, etc.; R11 = H, alkyl, alkoxy, Ph, cholesteryl, etc.; X = O, S, CH2, etc.; m = 0-90; n = 0, 1] are prepd. as drugs for enhancing host resistance against opportunistic infections in **AIDS** patients. 2-Acetamido-1,5-anhydro-4,6-O-benzylidene-2-deoxy-D-glucitol was reacted with L-2-chloropropionic acid in NaH-contg. dioxane to give 2-acetamido-1,5-anhydro-4,6-O-benzylidene-3-O-(D-1-carboxylethyl)-2-deoxy-D-glucitol. This was treated at -15.degree. with DMF, N-methylmorpholine, isobutyl chloroformate, and L-alanyl-D-isoglutamine benzyl ester-HCl to give 2-acetamido-1,5-anhydro-4,6-O-benzylidene-2-deoxy-3-O-(D-2-propionyl-L-alanyl-D-isoglutamine benzyl ester)-D-glucitol, which upon hydrogenolysis over Pd in HOAc gave 2-acetamido-1,5-anhydro-2-deoxy-3-O-(D-2-propionyl-L-alanyl-D-isoglutamine)-D-glucitol. I, administered s.c. at 100-300 mg/kg/day over 5 consecutive days, increased the prodn. of antibodies against bovine serum albumin in mice (no specific examples).

IT **81638-45-1P**